The Cape Town Stereotactic Pointer
Clinical Development and Applications

A Thesis submitted
in fulfillment of the requirements of the degree

Doctor of Medicine in Neurosurgery

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Table of Contents

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As our purpose was to develop a stereotactic system that would be applicable to any neurosurgeon, and not just someone with specific interest in stereotactic surgery, this system rapidly become widely used in our department and I am grateful to my fellow registrars during this period, Drs Andre Engelbrecht, Grant White, Susan Hattingh, David Welsh, David le Feuvre, David Carter, Tony Figaji and John Mugamba and to Professor Patrick Semple, all of whom performed cases and gave valuable input.

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Early in the development of the CTSP, access to literature was limited as much of the stereotactic literature wasn't available in South Africa. I was fortunate to spend a month learning about functional neurosurgery as the guest of Dr Peter Winkler at the Department of Neurosurgery at Grosshadern Hospital/ Ludwig Maximilian's University in Munich in July 1998. Much of the time was spent in their library reading around stereotaxis and I am grateful to the Taueber Family Trust for funding this.

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Writing a thesis is an immensely selfish undertaking and I am so grateful to Karen, Joshua and Liam for their endless love, support and encouragement. They showed limitless patience with my commitment to getting on with this in the midst of a few other tasks. It is to them I dedicate this thesis. One way or another, it's over and now we can ride to the mast.

Declaration

I, Anthony Graham Fieggen, hereby declare that the work on which this dissertation is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other University.

I empower the University to reproduce for the purpose of research either the whole or any portion of the contents in any manner whatsoever.

The work upon which this dissertation is based was approved by the Human Ethics Committee of the Faculty of Health Sciences of the University of Cape Town.

The author has no direct financial interest in the device described in this dissertation.

Signature: 

Date: 18. XI. 09

Abstract

This dissertation describes the development and clinical use of a novel stereotactic neurosurgical system, the Cape Town Stereotactic Pointer (CTSP). This system has four main components; a halo containing three fiducials also serves as the platform for a tripod pointing device which is set with the aid of a 3D phantom or a printed setting diagram, and software which enables transformation of imaging space into patient space.

Laboratory tests indicated an application accuracy of 1.9 +/- 0.6mm using the 3D phantom to set the tripod. From the first clinical application, the system underwent a series of iterations which could broadly be divided into four successive phases of refinement. This took place over a six year period, encompassing one hundred patients who underwent 115 stereotactic procedures.

Indications for surgery included biopsy (62.6%), aspiration (15.7%) and cannulation (21.7%) and the surgical objective was realized in 101/109 cases (92.7%). Given the fact that six of the eight failures represented errors of surgical judgment that could not be ascribed to the device, and each of two system errors resulted in a significant modification to the system, the CTSP demonstrated a satisfactory level of accuracy in the clinical setting.

This was accomplished at an acceptable complication rate, with one death five days after surgery attributable to a stereotactic procedure (mortality 0.9%) and major morbidity in two cases (1.7%); thirteen patients experienced minor complications, all of which proved to be transient (11.3%).

A simple protocol for use of the CTSP evolved over the course of this study, making it easier for neurosurgeons from varying backgrounds to introduce stereotaxis into their practice with the help of this system. In addition to satisfactory levels of clinical reliability and safety, the system was versatile and also well tolerated by patients. It is hoped that the CTSP provides a cost-effective alternative for neurosurgeons working in under-resourced settings. Sixty units of the production version of the CTSP have been sold and the system is now in use in ten countries.

Tables

Figures

Case Illustrations

Chapter 1

Introduction

Finding your way to an unseen destination depends on recognition of known landmarks- reliance on navigation is likely as old as vision itself. In the same way, the neurosurgeon needs to be able to find his or her way to lesions hidden within the depths of brain, reliably and safely. The conceptual framework that makes this possible is stereotaxis, a word derived from the Greek words stereo ("three-dimensional") and taxis ("arrangement").

This term was coined a century ago by Robert Clarke as he and Sir Victor Horsley developed a method for accurately passing probes into the brains of various experimental animals [Clarke]. A Cartesian co-ordinate system of section planes in three dimensions, sagittal, frontal and horizontal, was superimposed on the brain, dividing the intracranial space into eight segments (Figure 1.1). This hidden world was then explored with the help of a frame mounted outside the head, which was able to direct an instrument to a specific point in the brain defined in terms of these three dimensions [Horsley].

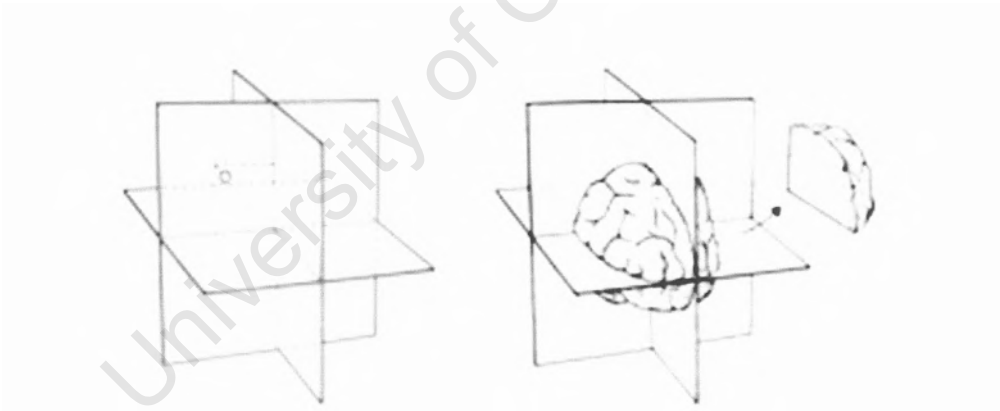


Figure 1.1: The Cartesian co-ordinate system comprises three planes intersecting at right angles, mathematically these are expressed as X-, Y- and Z-axes with each individual point having a unique set of X-, Y- and Z-co-ordinates. (from [Friedman_1992], permission requested from Wiley Interscience)

Stereotaxis has always been guided by images. Those used in the laboratory were derived from anatomical atlases and it took four decades before neurosurgeons were able to plot internal landmarks of the human brain with sufficient clarity to allow clinical application.

The pioneers in the field defined themselves as "stereotactic surgeons"; with remarkable ingenuity, they led the way in developing the first subspecialty in neurosurgery to be defined by a technology and not a disease [Bakay]. First guided by the shadows of pneumoencephalography and later by contrast ventriculography, they introduced a range of new techniques for exploring and modulating brain function.

It was however the ever-sharper outline of the brain revealed by computerized imaging that truly brought stereotaxis to the fore, to the extent that stereotactic guidance is now indispensable to the modern practice of neurosurgery. As one of the leading thinkers in the field has written, "stereotactic surgery has moved beyond a subspecialty, so that every neurosurgeon might benefit from using stereotactic techniques...." [Gildenberg_2000i]. There is no better example of this than the extent to which modern navigation technology has found its way into the Operating Theatre. Not only is image space mapped onto patient space, as with traditional stereotactic surgery, but patient space in turn can now be mapped back onto image space, extending the safe reach of the neurosurgeon.

No neurosurgeon who looks at a CT scan showing a lesion deep within the brain, whether an abscess to be tapped, a tumour to biopsy or a cyst to drain, should have to undertake this today without having the option of using a stereotactic instrument to guide his or her hand, using the so-called "freehand" approach.

While this may be true in the developed world, the "sad fact", to use the late Professor Ramamurthi's term, is that this is simply not the case in those parts of Africa, Asia and South America which have not enjoyed the benefits of this neurosurgical progress [Ramamurthi 2004]. Meagre investment by governments in healthcare, together with inadequate access to training for aspiring neurosurgeons and a perception that this is only for rich countries have limited the growth of our specialty in developing countries. The reality though is that neurosurgery does have much to offer in these countries, but will never gain a foothold without the "appropriate technology" that Ramamurthi sought.

Modern neurosurgical technology in the shape of operating microscopes, neuroendoscopes, stereotactic frames and navigation doesn't come cheap. Although increasing competition should help to drive prices down, this is still a niche market dominated by a few big companies and new applications and "add-ons" mean steadily increasing cost. Faced with our own lack of access to stereotaxis in Cape Town in the early 1990's, we were well aware of the limitations and hazards of freehand approaches and therefore receptive when an opportunity arose to improve matters.

This thesis will describe the development and use of a novel stereotactic system, the Cape Town Stereotactic Pointer (CTSP), which emerged from fruitful collaboration between land surveyors, biomedical engineers and neurosurgeons. Key considerations that informed this process were simplicity and cost; we sought to develop a stereotactic system that could readily be used by general neurosurgeons and was also relatively inexpensive, in order to encourage wider access to this fundamental technique. Achieving patient acceptance through considering their comfort was a concern but ultimately, accuracy would be of paramount importance.

As the essence of stereotaxis is the ability to locate the unseen target in the brain with the help of visible external landmarks, three components are required to ensure the surgical instrument finds the correct destination:

i. a "visible" reference framework, external to the brain
ii. an imaging system that will "see" both the reference system and the target within the brain
iii. a mechanical device that will enable one to reach that target, based on the external reference system.

After reviewing the history of stereotactic neurosurgery over the past century in Chapter 2, the evolution of the CTSP to meet these three requirements will be described in Chapter 3. As with all prototypes, the system went through various iterations before a clinically useful methodology emerged. As accuracy and precision are the hallmarks of stereotaxis, the various laboratory studies that underpinned the translation of this concept into the clinical arena will be reviewed in Chapter 4.

Chapter 5 describes the first one hundred patients who underwent 115 operations with this system over a 6 year period. As the development of the CTSP was of necessity also the development of stereotactic neurosurgery in Cape Town, the lessons learnt in developing the system as well as learning the principles of stereotaxis will be reviewed in detail.

Individual chapters will review specific applications. Stereotactic brain biopsy was overwhelmingly the most common procedure performed and this experience is covered in Chapter 6. Specific challenges will be addressed and the results obtained will be compared with the published literature with respect to diagnostic yield and complications.

Extending the spectrum of use through implantation of catheters for stereotactic chemotherapy

will be discussed in Chapter 7, where the method of stereotactic implantation of the catheter in the specific case of cystic craniopharyngioma will be examined, together with the results of this treatment strategy.

Chapter 8 encompasses a range of other applications, such as the use of the CTSP in children, insertion of shunts for treating hydrocephalus, aspiration of abscesses, biopsy in the setting of HIV, which is so relevant to South Africa and will conclude with a method of performing stereotactic craniotomy with the aid of the CTSP.

This thesis will conclude with an evaluation of the strengths and weaknesses of the CTSP in Chapter 9. One of our main goals in undertaking this project was to produce a system that was cost-effective and therefore available to a wider group of neurosurgeons, and the chapter will reflect on challenges in trying to meet this need. Modifications introduced by newer users, suggesting that this system is not only simple and easy to use but also versatile, will be described and future developments considered.

Appendices will cover the patient data and relevant forms, present a concise protocol detailing current clinical use and list the various ways in which this work has been presented.

Chapter 2

Historical overview

2.1 Origins

When surgeons first crossed the frontier into the human body, they were guided by a constellation of symptoms and signs pointing to a particular organ as the seat of the patient's trouble. The brain presented a particular challenge- not only was it protected by the rigid skull, but there were few clues to guide early surgeons until the pioneering work of 19th century neurologists such as Paul Broca and Hughlings Jackson led to an appreciation that different areas of the brain subserved specific and highly specialized functions.

In 1876, Broca was the first surgeon able to use a patient's neurological findings to localize an intracranial lesion, in this case an extradural abscess in the speech area, and treat it by a direct surgical approach [Green]. In a sense, modern neurosurgery was ushered in by an operation at the National Hospital for Nervous Disorders in London 125 years ago. A patient with focal seizures and a left hemiparesis was thought by his neurologist Alexander Hughes Bennett to have a tumour in the motor cortex on the right side of the brain. Bennett persuaded the surgeon Rickman Godlee that trephination in the right parietal area would allow resection and he produced a localization diagram in order to guide him; a tumour was indeed found just below the surface of the brain [Green]. This was perhaps the first instance ever of a neurosurgeon benefiting from navigation assistance!

Anatomists in the 19th century devised various instruments for guiding intracranial procedures, both in experimental animals and patients [Redfern]. Dittmar, working in Germany, reported using an instrument to guide probes into the medulla oblongata of experimental animals in 1873 and Zernov, Professor of Anatomy in Moscow, reported the use of an instrument called the "encephalometer" which was designed to identify cerebral convolutions and sulci for surgical procedures in 1889 [Kandel]. This was subsequently used on at least three occasions, one of which was to drain a brain abscess [Al-Rhodhan]. Another ingenious device for removal of missiles from the brain based on orthogonal X-rays was reported in a magazine called *L'illustration* [Benabid].

This era was also remarkable for the burgeoning interest in experimental neurophysiology with a great deal of animal experimentation conducted. The clinical landmarks used by the early

neurologists were soon supplemented by the new technique of X-ray radiography, which showed bone very well but was not at that stage able to reveal the anatomy of the brain. As will be seen, first neurophysiology and then neuroradiology would serve as springboards for the development of stereotactic neurosurgery.

2.2 Physiologists: Horsley and Clarke

Sir Victor Horsley (1857-1916), godson and namesake of Queen Victoria, was an extraordinary polymath (Figure 2.1). In addition to being a leading surgeon, intellectual and social activist, he was also a pioneering experimental neurophysiologist [Sachs]. He wished to elucidate the functions of the cerebellum by placing lesions in the deep cerebellar nuclei of Macaque monkeys and frustrated by his inability to do this accurately using a freehand approach, he enlisted the help of a surgical colleague, Robert Henry Clarke (1850-1921). Clarke solved this problem through combining two old concepts, a three-dimensional positioning apparatus and a Cartesian co-ordinate system [Pereira_2008i]. As already noted, a number of instruments had been utilized to guide various probes into the brain, but coupling such a device to a Cartesian coordinate system may truly have been an original concept [Kelly_2000i].

Clarke and Horsley divided the brain into eight segments by section planes in three dimensions-sagittal, frontal and horizontal, each of which was further divided at one millimeter intervals. Based on a series of meticulously taken sections at intervals of 2mm, they produced an atlas of the monkey brain in which each 1mm cube had a unique set of coordinates in these 3 planes [Clarke].

With this, they designed a "mechanical contrivance" capable of directing an electrode to any desired target within this coordinate system. This consisted of a brass frame, which could be affixed to the skull of an experimental animal by means of rods inserted into the external auditory meati. A headpiece was then attached to the frame; this contained an instrument carrier such as a micromanipulator and translational movement allowed calibration in each of the three axes [Dagi]. Their first such device, manufactured in 1905 by the London instrument maker Messrs Swift and Son, now resides in the Wellcome Collection at the Science Museum in London (Figure 2.1). They also devised various instruments for making electrolytic lesions in experimental animals and in applying their "combined method", were able to explore function in various regions of the brain. Their brief article in the *British Medical Journal* in 1906 was followed by a detailed report in *Brain* in 1908 [Horsley].

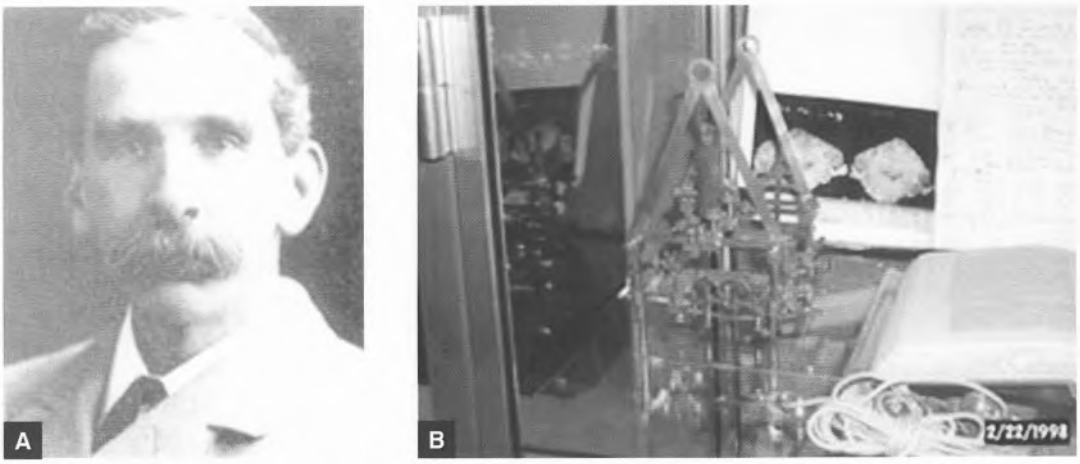


Figure 2.1: (a) Sir Victor Horsley. (b) The original Horsley-Clarke stereotactic apparatus (credit: Mr Paul Eldridge)

Clarke coined the term "stereotaxis" which was a hybrid derived from the Greek terms for "three dimensional" (stereo) and "arrangement" (taxis) [Dagi]. He was convinced that this device could be used on humans and predicted that with the use of this apparatus, "through a 5mm trephine hole, brain tumours might be treated by electrical means or by the placement of radium, relief of pain by coagulation of intracerebral tracts, and direct application of drugs and pharmaceuticals into the CNS" [Jensen]

It is puzzling that Horsley appears to have dismissed this possibility, leading to an acrimonious breakdown in their relationship. It has been suggested that a contributing factor may have been Clarke's envy of Horsley's position as the King's surgeon and he is reputed to have accused him of being a "self-seeking political wire-puller"! [Al-Rhodan]. Although Clarke subsequently became a general practitioner [Pereira 2008i], he remained interested in the field he had nurtured, continuing to work on various modifications of the device. He obtained a patent in 1912 and published a stereotactic atlas consisting of serial brain sections on which a co-ordinate grid was superimposed in 1920. It appears that he only published four papers, all of them concerned with stereotaxis [Kelly_1991].

A Canadian neurophysiologist, Aubrey Mussen was particularly impressed with the Horsley-Clarke apparatus, so much so that he purchased a model in 1906 for $100! [Olivier]. He had another frame built in London in 1918, modified for human use by calibrating it to external calvarial landmarks [Dagi], but was unable to persuade his surgical colleagues at the Montreal Neurological Institute to use this in the clinic.

2.3 Clinicians: Spiegel and Wycis

The major problem in the transfer of this technology from monkeys to patients was the much greater variability in the shape and size of the human cranium, together with considerable variation in the contours of the brain, particularly in the presence of atrophy or other cerebral pathology. Landmarks were required within the brain itself. The solution lay in technology already available- Roentgen's discovery of X-rays in 1895 was followed by Walter Dandy's introduction of air ventriculography in 1920, which for the first time allowed visualization of the living brain, even if only partially. Perhaps it is surprising that it took half a century for roentgenograms to find their way into the stereotactic operating room, but the impetus for this finally happening has been ascribed to the technological advances of the Second World War [Kelly_2000i]. This conflict stimulated the migration of stereotaxis from the laboratory into the operating theatre in various ways.

Ernst Spiegel, a Viennese neurologist born in 1895, was appointed professor of experimental neurology at Temple Medical School in Philadelphia in 1933. His interest in stereotaxis stemmed from a desire to find a less invasive alternative for the widely practiced procedure of pre-frontal lobotomy which necessitated a craniotomy and was replete with complications. He was also concerned with the treatment of movement disorders and before Clarke's death in 1926, he looked into having a stereotactic device manufactured by Swift, but the cost (£300) dissuaded him [Kelly_1991].

Spiegel established a remarkably productive collaboration with the neurosurgeon Henry Wycis, which culminated in the first human stereotactic operation, reported in Science in 1947 [Spiegel]. Their patient had Huntington's chorea and alcohol was injected into both the globus pallidus and the dorsomedial nucleus of the thalamus, with sustained benefit. Wycis verified the location of the lesion by performing an autopsy when the patient died 15 years later and then paid for his funeral! [Nashold 2004]

The frame used for this operation was similar to the Horsley-Clarke apparatus and was mounted on a ring suspended from a plaster cap made individually for each patient. After applying the headring with the base parallel to the Frankfurt plane, the patient was subjected to pneumoencephalography in order to identify the intraventricular landmarks which would be used to locate the target with the aid of a stereotactic atlas of the human brain which they had created. As the large volume of intraventricular air invariably made the patient acutely ill, the frame was usually removed and the operation planned for two days later.

The important point is that, for the first time, *internal* landmarks were used to tailor these operations to the patient's own anatomy, with intraventricular air serving as the first radiographic contrast medium. Spiegel and Wycis termed the new discipline "stereoencephalotomy." The key step was linking the patient's anatomy to one of several stereotactic atlases of the human brain which were developed over the years, such as that produced by Schaltenbrand and Bailey. The major problem was that there was still significant variability, which was not always adequately corrected by using ventricular landmarks.

Spiegel was productive throughout his career. He founded a journal in 1939 which was to serve as an important vehicle for the development of the nascent field of stereotaxis. The title, *Confinia Neurologica,* was true to his belief that he was working at the borderland of neurological understanding and he edited this journal until Gildenberg took over in 1975, renaming it *Applied Neurophysiology.* With the advent of image-guided surgery, the name of the journal was to change again a decade later, this time to *Stereotactic and Functional Neurosurgery.* Spiegel's final major contribution to the field was the book "Guided Brain Surgery" published in 1982, at the age of 87! [Gildenberg_2004].

2.4 The rise and fall of stereotaxis

A succession of neurosurgeons from around the world visited Philadelphia and in turn developed their own techniques, a feature of which was often a novel stereotactic frame, largely because no system had been produced commercially [Kelly_1991]. The market was still small and commercial viability was diminished by constant refinement of the various prototypes in response to new problems- the early stereotacticians certainly needed to be very innovative.

Among these enterprising pioneers, Lars Leksell (Stockholm), Jean Talairach and Jean Bertrand (Paris), Traugott Riechert (Freiberg), Hirotaro Narabayashi (Tokyo), Robert Rand (Los Angeles) and Ron Tasker (Toronto) were particularly prominent in stimulating the growth of stereotaxis around the world.

Lars Leksell (1907-1986) succeeded Herbert Olivecrona as Professor of Neurosurgery at the Karolinska Institute in Sweden. Although Leksell was determined to attempt stereotactic techniques wherever possible, he remained however committed to the notion of technical excellence in neurosurgery, believing that "the best stereotactic neurosurgeon is one who is also excellent in microsurgery" [Backlund 2004].

Leksell is a giant in the history of stereotaxis, having first developed the cuboidal target-centered frame which bears his name [Leksell 1949], he later consummated the marriage of stereotaxis and radiotherapy with the development of stereotactic radiosurgery, which is now one of the major applications of the stereotactic concept worldwide. He made his mark not only through the instruments he developed, but also in mentoring leaders of the next generation of stereotactic neurosurgery [Lunsford_1997].

Jean Talairach (1911-1993) had a somewhat different background, training initially as a neurologist and psychiatrist under Professor Marcel David at Ste. Anne. Like Spiegel and Wycis, he sought an alternative to frontal lobotomy and in the late forties designed his own stereotactic system with a double grid and relocatable cranial fixation system [Kelly 2004i]. He and Sabbaton also devised a system for collimated biplane teleradiography which improved accuracy by reducing magnification. There is no doubt that Talairach was an original thinker and Bertrand recollects a spat at the 1949 World Congress of Neurology between Spiegel and Wycis on the one side and David and Talairach over who had priority in the development of a human stereotactic apparatus! [Bertrand].

Patrick Kelly describes from first-hand experience how Talairach's group devised a process (repérage) whereby multiple data sources including ventriculography, stereoscopic angiography, serial biopsy and stereo-EEG were combined in scale drawings (les dessins) to provide a navigational chart of the patient's brain [Kelly_2004i]. It is noteworthy that they were able to perform tumour biopsies based on this painstaking process and also pioneer the use of interstitial irradiation where radionuclides such as iridium-192 were inserted into defined tumour volumes. Kelly later championed the role of stereotactic "volumetric" resection of tumours, crediting Talairach with teaching him that a stereotactic target was not necessarily a single point, but is also a volume in space.

It is interesting to reflect on the fact that an important driver in early stereotactic neurosurgery was the quest for improved psychosurgery. It wasn't long before other indications became more prominent, most notably movement disorders, pain and epilepsy. As is usually the case, this new discipline culminated in an international society with the International Society for Research in Stereoencephalotomy established in 1961. This was renamed the World Society for Stereotactic and Functional Neurosurgery (WSSFN) at the meeting held in Tokyo in 1971; it is also worth noting the decision at that meeting to replace the term stereotaxic with stereotactic ("to touch") to refer to human surgery, reserving the older term for the laboratory [Gildenberg_1993].

Although Spiegel and Wycis had pointed to these wider applications, such as aspiration of tumour cysts in their 1947 article, virtually all operations done in the early days were for movement disorders such as Parkinson's Disease. The advent of an effective medical treatment in the form of l-dopa in 1967 led to a dramatic fall in the number of stereotactic operations over the next decade (Figure 2.2) [Gildenberg 1987]. Kelly credits Spiegel's protégé, Philip Gildenberg, with keeping "the torch of American stereotaxy burning through the post l-dopa dark ages"! [Kelly 2004i]

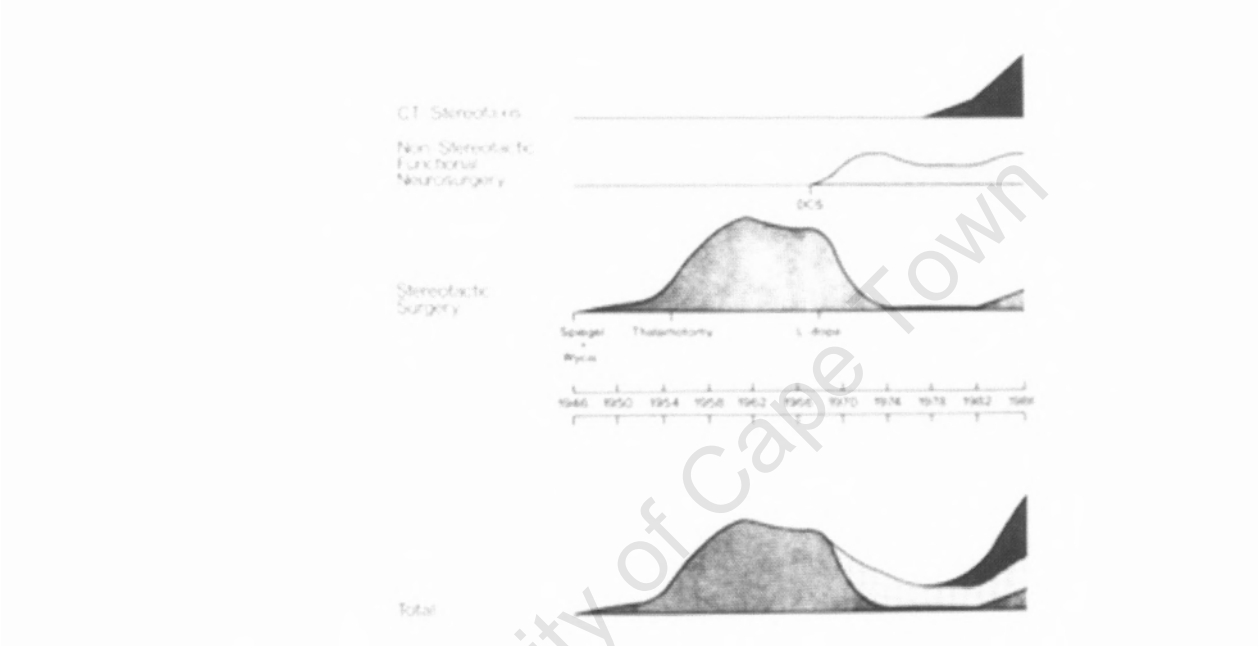


Figure 2.2: Variation in the levels of activity in stereotactic and non-stereotactic functional neurosurgery from the time of Spiegel and Wycis first stereotactic surgery in 1946, graphically showing the decline in stereotactic surgery following the introduction of I-dopa, followed by a second upsurge of interest in the 1970s (from [Gildenberg_1987], with permission from Williams and Wilkins).

Two developments were to bring a new dawn for stereotaxis. It wasn't long before the shortcomings of long-term l-dopa treatment became apparent, with many patients developing troublesome side-effects, but more importantly, computerized tomographic scanning was about to make its entrance.

2.5 Tomography and the resurrection

Human stereotactic surgery and computers are age mates, with the first electronic calculator introduced just a year before Spiegel and Wycis reported their first case [Kali]. The impact of

computers on this field was to be enormous; the history of stereotaxis offers an excellent example of the migration of technology into neurosurgery, and indeed into the practice of medicine as a whole [Dagi]. Spiegel and Wycis had taken advantage of post-war advancements in plane film radiology but it was really the advent of computerized axial tomography, also known as computed tomography (CT) that launched stereotaxis into the mainstream of neurosurgery.

The Nobel Prize in Physiology or Medicine for 1979 was awarded to Allan MacLeod Cormack and Godfrey Hounsfield in recognition of their work in the development of computerized tomography. While working as a physicist in the Radiotherapy department at Groote Schuur Hospital in the 1950's, Cormack was required to calculate the radiation doses given to patients. In his Nobel Prize citation, Professor Greitz noted that the methods in use at the time had been imprecise and Cormack devised a mathematical solution for obtaining precise values for the tissue-density distribution within the body, which he realized could also be used to produce X-ray images of cross-sectional slices of the body [Vaughan]. Unfortunately, performing the calculations required was beyond the capacity of most computers of the day.

Hounsfield came to this field from a very different direction; he hit on the idea of CT while contemplating the potential of automatic pattern recognition in clinical practice [Petrik]. At the time, he was working for Electrical and Music Industries (EMI), and he was fortunate in finding an ally in the neuroradiologist at Atkinson Morley's Hospital in London, Dr James Ambrose. Ambrose, a South African who had found himself in the UK as a Spitfire pilot, immediately saw the clinical potential of this concept, a prototype was installed at his hospital and the first patient was duly scanned on 1 October 1971.

The most obvious advance signified by CT was the ability to *directly* visualize intracranial structures other than just the ventricles and vessels. Normal anatomical structures such as the white matter and basal ganglia could now be visualized, as could a wide array of pathological entities such as haematomas, abscesses and tumours. Equally important though was the fact that this new imaging medium was also an accurate 3D measuring device as it was *spatially accurate,* using a measuring system based on a Cartesian co-ordinate system. Although CT reduced the problems of parallax, magnification and proportion which plagued teleradiography, some new technical challenges arose, such the need to include frame fiducials for purposes of co-ordinate mapping while avoiding large metallic artifacts. Initially it was laborious to get the coordinates off the CT slice as each slice had to be "transferred" onto stereo X-rays, but various groups tackled these problems in different ways.

Bergstrom and Greitz reported adapting the Leksell frame for CT as early as 1976 [Bergstrom], but this required a thermoplastic head cast and was soon abandoned [Dagi]. One of the challenges was to find a way of registering the z co-ordinate on each image. Theodore Roberts, Professor of Neurosurgery at the University of Utah encouraged a medical student, Robert Brown, to tackle this problem [Cosman]. His simple but elegant technique incorporated the localizing device into the stereotactic apparatus itself, with three diagonal rods in an "N" shaped array generating fiducials on each CT scan slice [Brown]. This was incorporated into a number of other systems. Perry and co-workers at Pfizer independently developed an artifact-free frame along similar lines [Perry]. Leksell himself devised a solution [Leksell_1980], as did Gildenberg, in which the CT slice was related to a lateral X-ray film in the operating room [Gildenberg_1982].

2.6 Proliferation

There was a remarkable proliferation of stereotactic systems- this reflected not only the ingenuity of the early stereotactic surgeons, but also the reality that the field had to develop before commercial vendors would consider it viable to produce these instruments.

Devising a widely quoted classification, Gildenberg noted that each stereotactic apparatus fell into one of four different groups, depending on how the electrode carrier was mounted:

1. **Translational** systems, such as Horsley-Clarke and Spiegel-Wycis, and the Talairach system.

2. **Arc or polar coordinate** system, employing an electrode carrier fitted to an arc such that it always points to the centre of the frame- this was the novel contribution of Leksell. Other arc systems include the Todd-Wells and Riechert-Mundinger.

3. **Burr-hole mounted** systems consist of a fulcrum attached to a burr-hole, to which is fixed an electrode carrier with angular adjustments to point to the target and a microdrive to advance the electrode- the McKinley and Patil systems are examples.

4. Early in the era of CT scanning, the availability of computers made possible some rather complex systems consisting of **multiple interlocking arcs,** such as the Brown-Roberts-Wells (BRW frame); this was later simplified as the arc-centered Cosman-Roberts-Wells (CRW frame).

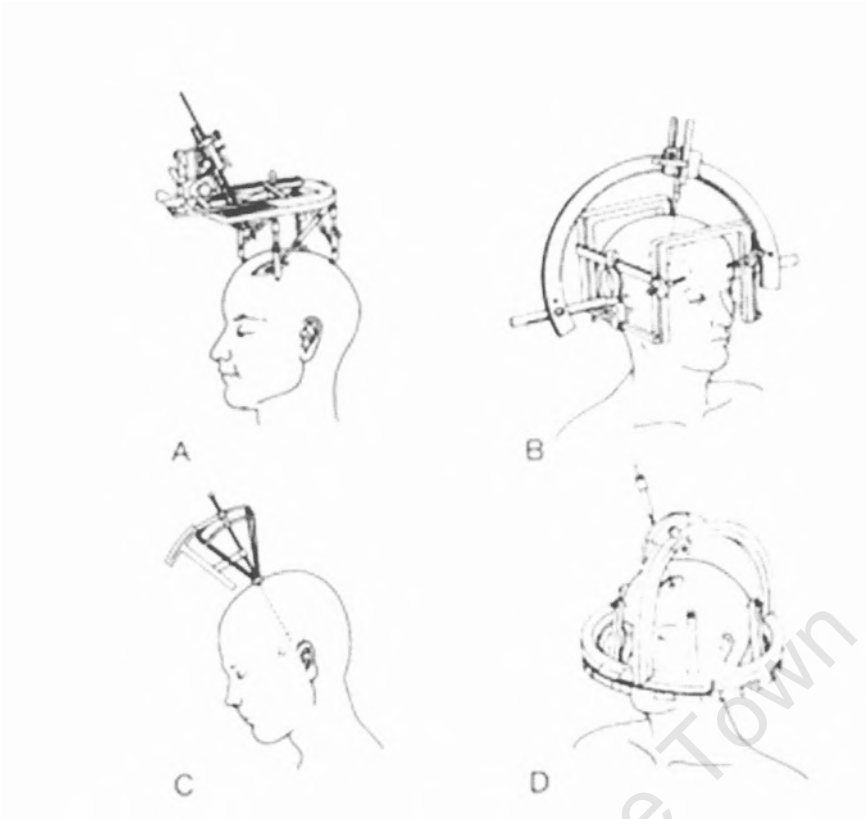


Figure 2.3: The four basic types of stereotactic apparatus. A: Translational system. B: Arc system. C: Burr-hole mounted. **D:** Interlocking arcs (from [Gildenberg_1987], with permission from Williams and Wilkins)

One of the more helpful innovations was Mundinger's use of a phantom target device to mechanically set the stereotactic frame to the correct trajectory and depth, with the phantom replicating the "patient space". The evolution of the BRW into the CRW arc-centered system is an excellent example of how a surgical apparatus improves as new challenges are met [Pell_1994i]. The successful systems did very well- over 2,500 Todd-Wells frames were sold and up to a decade ago, approximately 2,000 BRW frames, 2,500 CRW frames and 1,500 Leksell frames had been produced [Apuzzo 1999].

2.7 Attempts to simplify stereotaxis

With the advent of CT, a number of simple stereotactic systems were introduced. Some were based on the "plane-of-target" concept which required that the device be aligned in the CT scanner such that the entry point is on the same image slice as the target, but this severely limited the range of safe trajectories [Friedman 1988]. Various techniques for scalp marking using CT were proposed [Patil, Hirschberg], but none of these concepts were truly stereotactic.

In an attempt to broaden access to stereotaxis, Carol introduced a simple skull-mounted stereotactic system (the Pelorus Frame) which employed a skull set consisting of a series of discs, the first of which was attached with two self-tapping screws; the patient was secured to the CT table via a table mount attached to the skull mount [Carol 1985]. A novel three-dimensional phantom (the "Gyrantom") was used to simulate the relationship between the intracranial target, the entry point and the skull and efficacy was demonstrated in a clinical series [Carol 1987].

A number of non-invasive stereotactic systems have been introduced, most notably the Multipurpose Stereoadaptor [Laitinen_1987], which was shown to be effective and efficient in a series of 18 patients [Hariz] and the Gill-Thomas relocatable frame from Queen's Square [Gill] which is particularly applicable to stereotactic radiotherapy. A group in Australia described the use of stereolithography to create a solid plastic model (a "biomodel") which facilitated planning of surgery which was guided by a three-legged frame containing a ball-and-socket instrument guide [d'Urso].

The high cost of the instrumentation was a major obstacle to neurosurgeons introducing stereotaxis in developing countries; in China, Dr Jian-Ping Xu and Dr Da-Jie Jian both designed their own systems of necessity [Sun] and Dr Arjun Sehgal played a very important role in the development of stereotaxis in India through the introduction of a new stereotactic apparatus [Ramamurthi_2000].

2.8 The new challenge: MRI

Magnetic Resonance Imaging was introduced into clinical practice within a decade of CT and the first report of its use for stereotactic neurosurgery appeared in 1983 [Thomas 1983]. Clinicians immediately appreciated the advantages of this new imaging technology, the most striking of which was the ability to now obtain images in all three planes (corona) and sagittal in addition to the axial images rendered by CT). The ever-improving differentiation of soft tissues such as brain produced exquisite images of the central nervous system, including the spine and contrast enhancement with gadolinium delineated pathology with greater clarity than CT.

Early disadvantages included long scan times, enormous cost and the absolute proscription of any ferromagnetic metals, which necessitated the development of a new generation of MRI-compatible stereotactic frames. Despite the obvious superior quality of the images produced, reservations arose concerning possible geometric distortion which would compromise the validity of fiducial localization [Sumanaweera].

MR imaging uses a strong, constant magnetic field (BO) and three pulsed linear magnetic field gradients (magnetic fields that change in a linear fashion over distance) to localize and to image points in an object. Geometric distortions occur when the constant field and the gradient field are perturbed from their ideal character; causes include gradient field non-linearities and resonance offsets due to chemical shifts or due to magnetic field inhomogeneities [Sumanaweera]. Of these, the two most important are gradient field non-linearities and magnetic field inhomogeneities induced by the imaged object. An early solution was to modify the frame so the patient could undergo both CT and MRI [Lunsford_1986], leading to the development of "image-fusion" techniques, where the accuracy of CT was wedded to the superior images of MRI. A comprehensive study reported a difference of 2mm between stereotactic co-ordinates determined by CT and MRI [Kondziolka_1992], but current MRI technology appears to have addressed most of these problems and many neurosurgeons now use this imaging modality alone.

2.9 From frameless to robots

Although a frame had become almost synonymous with stereotactic surgery, this was simply a means to an end, with the essential feature being defining a co-ordinate system based upon the patient's image and the patient's anatomy [Bakay]. Once that had been accomplished, transformation and co-registration of these two co-ordinate systems allowed a point in imaging space to be related to anatomical space (and, as we shall see, vice versa).

Although stereotactic frames provided a stable and redundant frame of reference as well as a stable aiming arc, they had disadvantages, including restriction of the operative field, bulk and complexity. Furthermore, the frame was always temporary and there was no real-time updating after the initial scan [Maciunas_1993]. A number of centres described innovative approaches to utilizing stereotactic guidance without need of a frame, such as the "Neuronavigator", a stereotactic articulated arm from Tokyo [Watanabe] and integration of the microscope in Lebanon, NH [Roberts], where the term "frameless stereotaxy" appears to have originated. Likening the ongoing usage of this term to that of "horseless carriage" to refer to the automobile, Maciunas later argued for the adoption of the term "interactive image-guided surgery" [Maciunas_1993]. In extending the analogy, he cogently reasoned that the engine driving this new technology was the digital computer.

As most surgical interventions are preceded by imaging of some kind, one could argue that all modern surgery is "image guided", but in true image-guided surgery, the images are used

quantitatively- in other words, their spatial parameters carry equal or greater weight than their grey-scale parameters [Galloway_2001]. A detailed review of the evolution of this metamorphosis in stereotaxis would be out of place here, but this technology has really placed stereotactic methodology squarely in the midst of mainstream neurosurgery in the form of surgical navigation.

Today, it would be unusual to find a neurosurgical department in any developed country that didn't have access to at least one BrainLab® or StealthStation®. While the appeal of navigation is clearly apparent in open surgery, some authors have even suggested that such approaches are superior to frame-based approaches for closed procedures such as biopsies [Dorward_2002]; this argument does, however, need to take into account the long-established track record of frame-based approaches, which have set a benchmark [Lunsford 2008]. The culmination of the quest for real-time co-registration of patient space and image space is utilization of intraoperative imaging such as ultrasound [Unsgaard] or even MRI [Sutherland]; perhaps robotic assistance is the next step in this continuum [Louw, DF].

2.10 Functional Stereotactic Neurosurgery

The advent of sectional imaging, first CT and then MRI, opened up a whole new spectrum of so-called "morphological" indications for stereotactic neurosurgery, many of which were diagnostic in nature. The core interest of the discipline however has always been investigating and modulating the physiology of the central nervous system, in treating "functional" conditions such as movement disorders and pain. As the purpose of the CTSP was to meet the needs of the general neurosurgeon confronted with diagnosing and treating a lesion found on a scan, space does not permit a detailed review of the fascinating history of functional stereotactic surgery.

Although no CT-based stereotactic surgery was being performed in Cape Town when this work commenced, a number of functional cases had been performed some years previously by the first Helen and Morris Mauerberger Professor of Neurosurgery, JC "Kay" de Villiers. He had been trained in this field at Atkinson Morley's Hospital in London and was assisted in his endeavours by Dr Peter Keet [de Villiers JC, personal communication].

Early surgical interventions were predominantly ablations targeting a wide array of brain regions; although these were primarily guided by imaging such as ventriculography, microelectrode recordings were often used as well. Although thalamotomy became a popular procedure for controlling tremor, this fell from favour following the introduction of l-dopa [Gildenberg_1987]. The recognition of drug-induced complications, together with the reintroduction of pallidotomy

by Laitinen's group [Laitinen 1992] led to a rebirth of surgery for Parkinson's Disease [Gildenberg 2005].

A reversible alternative for these patients became available with introduction of deep brain stimulation, largely through the pioneering work of Alim Benabid. Although the mechanism of action is still not fully understood, electrodes placed in the ventral intermediate nucleus of the thalamus markedly improve tremor, while those in the internal segment of the globus pallidus or the subthalamic nucleus substantially improve bradykinesia, rigidity and tremor [Perlmutter]. This is currently a vibrant area of research with a bewildering array of brain regions now targeted for conditions ranging from dystonia and pain through to depression and other psychiatric conditions.

2.11 What is Stereotactic Neurosurgery today?

The literature pertaining to the development of stereotactic surgery is vast; although there has been a concerted attempt to cover this adequately, it must be mentioned that to a great extent only the English-language literature has been accessible to the author. This is an unfortunate limitation in that much of the innovation in this field has originated in Europe, but it may be safe to assume that most of the important information has permeated across barriers of language.

For the General Neurosurgeon, a stereotactic system remains simply a surgical guidance device and although the mechanics of this have evolved dramatically over a century, the underlying concept remains unchanged. The challenge is figuring out where to point this device and that is where modern imaging has had such a dramatic impact.

During the century since Horsley and Clarke introduced the concept of stereotaxis, enormous technical strides have enabled neurosurgery to evolve rapidly. It is clear from this review that many of the new methodologies that have been adopted throughout neurosurgery, such as frame-based and frameless procedures for biopsy of lesions, neuronavigation during open surgery and radiosurgery, have their origins in this concept.

Within this context, the European Society for Stereotactic and Functional Neurosurgery (ESSFN) and the WSSFN have published a consensus definition of contemporary Stereotactic and Functional Neurosurgery [WSSFN]:

"Stereotactic and Functional Neurosurgery is a branch of neurosurgery that utilizes dedicated

structural and functional neuroimaging to identify and target discrete areas of the brain and to perform specific interventions (for example ablation, neurostimulation, neuromodulation, neurotransplantation, and others) using dedicated instruments and machinery in order to relieve a variety of symptoms of neurological and other disorders and to improve function of both the structurally normal and abnormal nervous system."

As with all branches of modern neurosurgery, Stereotactic Neurosurgery has quite clearly evolved into a highly specialized field. This process of refinement has invariably been accompanied by increasing technical sophistication, which inevitably comes at a greater cost. This creates a difficult tension for neurosurgeons practicing in under-resourced regions of the world, torn between knowing they could be doing a better job, and the reality of the patients needing treatment now. One of the greatest challenges in modern neurosurgery is finding ways of bridging this gap.

Chapter 3

Development of the Cape Town Stereotactic Pointer

3.1 Overview of the CTSP

All stereotactic frames share the common purpose of establishing a rigid relationship between the outside of the patient's head and the brain inside in order to provide a mechanical outside space guidance system [Adams 1998].

For a stereotactic system, the essential requirements are:

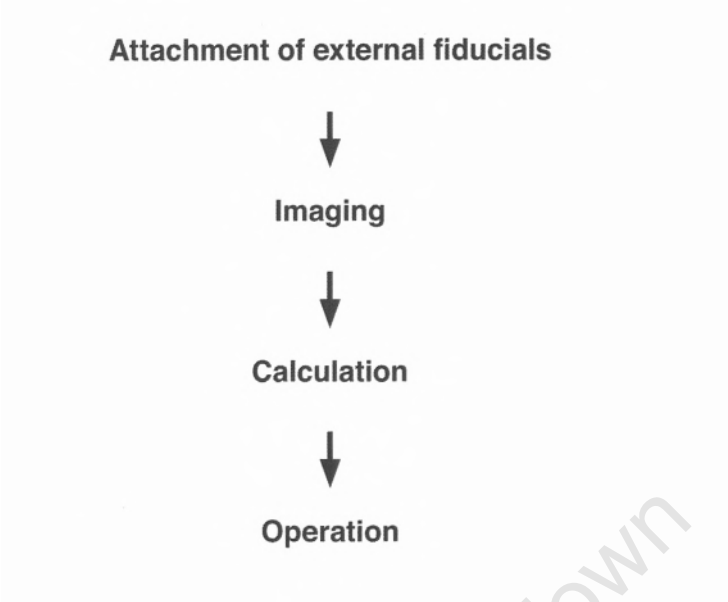
i. an external constellation of visible fiducials
ii. a computer program that enables one to transform the three-dimensional space of the visible fiducials into the three dimensional space of the invisible brain.
iii. a construct which replicates the patient's own three dimensional space
iv. a surgical guidance device

In the specific case of the CTSP, these requirements are fulfilled by the following components:

i. a halo incorporating three ball bearings; these serve as the fiducials which are visible both externally and on imaging with a CT scanner
ii. computer software developed by Adams and van Geems and licensed to Fibretek
iii. a three dimensional phantom
iv. a three-legged or tripod stool with a swivel head

Figure 3.1: The first production version of the CTSP, showing the full set of components required to use the CTSP, including a laptop computer.

There are four discrete steps in the use of the CTSP:



As with any other stereotactic system, one also requires:

- an imaging system which will show both the fiducials and the area of surgical interest (typically a CT scanner)
- various surgical tools such as biopsy cannulae, catheters an electrodes.

This chapter will examine the concept underlying the Cape Town Stereotactic Pointer, which was rooted in the discipline of photogrammetry. From its origins as a proton beam placement method, this concept then evolved through various surgical iterations, undergoing a metamorphosis from a rather complex stereophotogrammetric-controlled surgical pointing device to a simple and effective neurosurgical apparatus.

3.2 Beacons in the Brain

Few people have driven past a land surveyor busy with his or her theodolite and not wondered what exactly they were up to. When performing a boundary survey on a property, they are required to locate the original property beacons, some of which are "lost", with reference to the existing integrated survey system which already exists, based on a network of visible trigonometric beacons. Prior to the advent of the Global Positioning System (GPS), the cadastral surveyor had a well-drilled routine that was invariably successful.

As Adams [1999] has written, "the "lost" beacon was located by setting up a theodolite in the vicinity, observing a round of angles to three or more trigonometric pillars, undertaking a resection calculation and a transformation of coordinates of a local origin system into the integrated system, turning off a pre-computed angle, taping a pre-computed distance, digging a hole and revealing a rusty old iron pin or angle iron that had been hidden from sight for numerous years". Sounds a bit like neurosurgery doesn't it?

This project arose out of a discussion between Professor Jonathan Peter, at the time the newly appointed Chair of Neurosurgery at the University of Cape Town (UCT), and Emeritus Professor Laurie Adams, who had taken up a research position in the Department of Biomedical Engineering after retiring from the Chair of Land Surveying at UCT. Professor Peter and two of his registrars, Dr Graham Fieggen (the author) and Dr Allan Taylor, were looking to develop a stereotactic system to locate targets in the brain, with a particular interest in finding a way to insert shunt catheters accurately in the ventricle. Professor Adams saw this as a straightforward land surveying problem, entirely analogous to the "lost" boundary beacon situation and he enlisted the help of one of his postgraduate students Ms Barbara van Geems, who tackled this as a PhD project [van Geems].

Figure 3.2: Professor Laurie Adams (Picture credit: Monday Paper)

Adams had previously considered the problem of locating anatomical points using X-rays, in this case X-ray stereoscopic pairs [Adams1 981]. In mathematical terms, an X-ray picture represents the mapping of space upon a plane which is a special case of a central projection; in other words, an X-ray picture represents the projection of 3-D space onto 2-D film. It is therefore not possible to recreate the position in space of objects imaged on an X-ray picture by using a single picture, but if two pictures are taken of the same object from slightly different points of view, then it is possible to recreate the relative position in space by various means. The technique for

measurement in X-ray photographs is known as X-ray photogrammetry and is primarily used for determining geometrical data such as the size, position and shape of objects.

Adams described a method using stereophotogrammetric techniques that enabled one to locate an "intracranial" target located within a polyurethane model head [Adams 1981]. Although this system was highly accurate, with vector displacement errors of less than 1mm between calculated and control co-ordinates, it was limited by the fact that the target could only be reached along a trajectory that was orthogonal to the surface (i.e., there was only one possible trajectory). Furthermore, all marker coordination was done using stereo X-rays and stereophotogrammetry which is very labour intensive and time-consuming and therefore unsuitable for routine clinical practice [van Geems].

It is of interest to note that the theory of stereophotogrammetry was first postulated by the French-born scholar HG Fourcade in a paper read before the South African Philosophical Society in Cape Town in 1901. Following publication of this method [Fourcade], he produced the first recorded topographic map using stereoscopic measurements [Adams_2001]. In a remarkable co-incidence in relation to the work covered in this thesis, the map he produced depicted Devil's Peak in Cape Town, on whose slopes the Medical School of the University of Cape Town was founded in 1912 [Louw, JH].

3.3 Radiosurgical Roots

The advent of stereotactic radiosurgery has already been mentioned, with various stereotactic systems being modified to guide the delivery of radiation. The CTSP may well be the only stereotactic system where the reverse occurred.

Radiotherapy can be administered using either photons or protons. Both modalities are very effective at killing tumour cells but are limited by the damage done to healthy surrounding tissue, which is particularly relevant in the brain. As was mentioned in the profile of Lars Leksell, one of his many brilliant contributions was the concept of using the precise guidance of stereotaxis to direct single high doses of radiation to various loci in the brain [Leksell_1951]. This become known as stereotactic radiosurgery and may be accomplished with two different techniques:

- Multiple X-ray beams (photons) converging to a single point
- The Bragg peak effect of heavy particles (protons)

Photon based therapy is exemplified by two different systems, the Linear accelerator (LINAC) and Gamma Knife and has achieved much wider application than Proton therapy, which requires an extremely costly cyclotron. The South African National Accelerator Centre was commissioned at Faure in the Western Cape in 1986; the cyclotron at this facility, 35 km from downtown Cape Town, was designed to produce high-energy particles for nuclear physics research, radioisotope production and radiation therapy with either neutrons or protons. The latter function made it the only heavy particle facility in the Southern hemisphere, servicing patients referred through Groote Schuur, Red Cross Children's Hospital and Tygerberg Hospital; this facility is now known as iThemba Laboratories.

The main accelerator is a variable-energy separated-sector cyclotron capable of producing a 200MeV horizontal beam [Jones]. Protons have a similar biological effect to conventional RT and are attractive for treating lesions in the brain due to their dose-distribution with a low dose at the surface, a peak at a predictable depth and an abrupt distal drop-off (the Bragg peak). As it is not possible to "bend" a proton beam which is therefore in a fixed location, the tumour is placed in the correct location by translating and rotating the patient [Adams_1999].

Adams and Ruther of the Departments of Surveying and Geodetic Engineering and of Mechanical Engineering of the University of Cape Town devised a unique stereophotogrammetric patient positioning system [Adams_ 1989]. The system they devised not only moved the patient into the correct position, but also monitored for any unwanted movement using multiple charge-coupled device (CCD) cameras.

The basic principal of the stereophotogrammetric positioning system is that the 3-D co-ordinates of an invisible point may be described by its position in space based on fixed and visible landmarks. In the case of a lesion in the brain, these landmarks could be located either on the scalp or housed in a frame firmly attached to the head and this orthogonal 3-D coordinate system was established most easily through CT scan or MRI. A patient referred for proton therapy would undergo a planning CT scan wearing a snug custom-made mask, which contained a number of 1mm radio-opaque targets or fiducials. Following the scan, retroflective markers are fixed to the mask exactly over the fiducials. The mask was then fixed to the specially designed chair in which the patient sat for proton therapy; this chair has 5 degrees of freedom (three translations and two rotations), enabling precise placement of the tumour in the path of the fixed horizontal proton beam. This was surrounded by an array of 5-6 black and white CCD cameras connected to a frame-grabber, capturing video images which were analyzed on a personal computer (PC) linked to a second PC which controlled the chair. The purpose of this was to detect any

patient movement after commencement of treatment so that the beam could be cut immediately [Adams_1989].

This procedure, termed the "biostereometric method", was found to have a high degree of accuracy with the mean displacement of the fiducials in the order of 1.0 mm [Levin].

Figure 3.3: Patient undergoing proton therapy at the National Accelerator Centre; the fiducials are clearly seen (credit: Dr JD Parkes)

3.4 Stereophotogrammetry in the Operating Theatre

If one thinks of the proton beam as a surgical instrument (as is implicit in the term "gamma knife" for an equivalent photon beam), it is readily apparent that this methodology could also be used to guide the surgeon's hand in locating invisible "targets".

Professor Laurie Adams presented his work to a meeting of senior academics in the Faculty of Medicine at UCT in 1993. He suggested that this technique could be used much more widely and encouraged clinicians to collaborate with him in developing a stereophotogrammetric-controlled pointing device (SPD) for surgical use. Professor Jonathan Peter, newly appointed Chair of Neurosurgery saw a potential application of this concept in guiding the insertion of ventriculo-peritoneal shunts for treating hydrocephalus. The proximal catheter, which is inserted into the ventricle, must not only enter the ventricle, but must also follow the correct trajectory so that the tip is correctly located; this is therefore a vector which can be described in terms of proximal and distal points.

A project to devise a SPD method that would guide the neurosurgeon in placing shunts optimally was commenced; an additional aim was to be able to correct for any patient movement during the planning CT scan. The reason for this was most of the patients for whom this system was intended were young children and this was considered a potential alternative to sedation.

The Proton therapy system required a number of modifications as a mask was clearly impractical for surgery; four fiducials were therefore attached to the scalp around the region of shunt insertion. Two CCD cameras were mounted on a portable trolley, which also had a frame grabber, PC and electronic laser-pointing device. This low power laser was able to demonstrate the vector from the surface towards the intracranial target, thus guiding insertion of the shunt catheter in the correct trajectory.

Before surgery, the cameras had to be calibrated using a surveyed control framework [van Geems]. While this was not a great obstacle, having the fiducials in the operative field certainly was, particularly with shunt surgery where sterility is paramount. Furthermore, the laser presented logistic and space disadvantages in the Operating Room. The solution to these challenges was a simple, small manual pointing aid in the form of a tripod, which could be preset outside the Operating Room. The first prototype, the "J1" was a particularly small three-legged device, which was very unstable and clearly unsuitable; although the system was conceptually elegant and a subsequent iteration (Figure 3.3) was more promising [Adams_1995], this system was never used clinically.

Figure 3.4: An early version of the Pointer ("J3") mounted on the phantom head used for various accuracy trials. The tip of the probe is co-incident with the target "intracranial lesion".

An important consequence of this phase of the project however was the realization that the CCD cameras were in fact no longer required. Adams labeled this development somewhat paradoxically as "photogrammetry without cameras" and the stage was now set for the emergence of a system that truly would work in the Operating Theatre.

3.5 The principles of the Cape Town Stereotactic Pointer

The mathematical concept

The CTSP is based on the same principle outlined above, namely that the known three dimensional coordinates of a point in space obtained from one coordinate system (X,Y,Z) can be described in terms of a second coordinate system (x,y,z) provided that the spatial relationship between the two systems is known [Adams 1998].

This relationship can be obtained by using markers that can be visualized and co-ordinated in *both* systems, for example, radio-opaque targets such as the ball bearings attached to the patient's head. Using an imaging system such as a CT scanner, one can co-ordinate the *invisible* intracranial target with these *visible* external markers or fiducials in three dimensions (X, Y, and Z).

The "equivalent" external fiducials (the three foot points of the tripod) can also be co-ordinated in the second system (x, y, z), which has been previously calibrated. In the case of the CTSP tripod, this calibration was undertaken using a reflex microscope, a highly accurate instrument with a measuring precision of +/- 4 micrometers in all three axes [Scott, PJ].

The co-ordinates of the intracranial target, which have been obtained from the CT image, can readily be transformed mathematically into the CTSP system [Adams_1999], using a centre of gravity relationship of common points by the matrix relationship:

$$\begin{bmatrix} X' \\ Y' \\ Z' \end{bmatrix} = R^T \begin{bmatrix} X \\ Y \\ Z \end{bmatrix}$$

Where

X, Y, Z' = the three dimensional co-ordinates of a point in system A

X, Y, Z = the three dimensional co-ordinates of a point in system B

RT = the Rodrigues matrix

The design concept

The surgical guidance device is a tripod which defines two parallel planes intersected by a vector (Figure 3.5).

A plane is defined by any three points in 3D space which are not collinear and for this device, the three footpoints constitute one plane (the distal plane) while the other is swept out by rotation of the horizontal arm containing the surgical instrument guidance device (the proximal plane), which is parallel to the distal plane. As these planes are a fixed distance apart, this distance is known.

A vector, that has an initial and a terminal point, has both magnitude (length) and direction. If a burr hole has been drilled in order to reach an intracranial target, the line passing from defined target to the burrhole constitutes a vector.

For the CTSP tripod, this surgical vector can be continued out into space to intersect the two planes defined by the footpoints and the instrument guide. As will be described, the points at which this vector intersects both of these planes are the basis of the scaled graphical plot which is used to set the tripod to the correct trajectory to locate this intracranial target [Adams 1999].

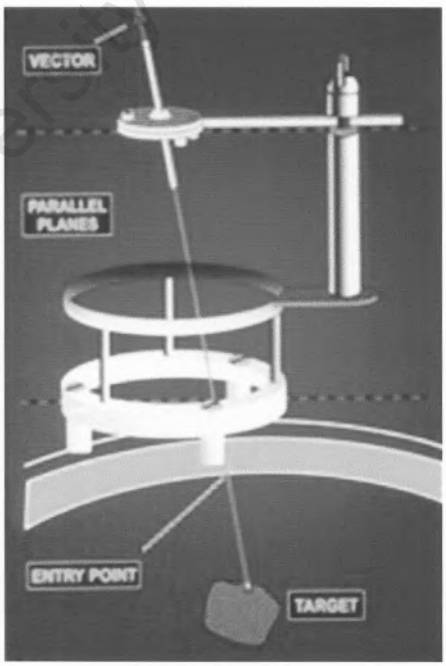


Figure 3.5: An early cartoon showing the design principles of the CTSP, with two parallel planes described by the footpoints and the horizontal arm, intersected by a vector described by the instrument carrier. This vector is defined by the trajectory through two points, namely the intracranial target and the burr hole or "entry point".

3.6 The components of the CTSP

As mentioned at the start of this chapter, the CTSP comprises the following components:

- a halo incorporating three ball bearings; these serve as the fiducials which are visible both externally and on imaging with a CT scanner
- computer software developed by Adams and van Geems, now licensed to Fibretek®
- a three dimensional phantom
- a three-legged or tripod stool with a swivel head

Before describing the role and development of each of the four specific components, it is worth considering the central role played by the CT scanner, correct use of which is fundamental to obtaining a homogenous and therefore accurate set of spatial co-ordinates for the fiducials and the intracranial target.

3.6.1 The scanners

For all the scanners used in this study, the axial image reflected the X and Y axes, with the X axis running in the corona! plane (i.e. from side to side) and the Y axis running in the sagittal plane (i.e. front to back/ back to front). The origin of the axes (i.e. X=0; Y=0) was in the centre of the screen and it is absolutely crucial not to shift the image in relation to this, or to alter the position of the co-ordinate grid. The X and Y co-ordinates to an accuracy of 0.1 mm for any discrete point on the axial image could readily be obtained by activating the screen cursor and manually positioning this on the selected target, with an accuracy of 0.1mm. Movement of the table is along the Z axis which runs in the axial plane caudally (i.e. from head to foot) and the table position, which is displayed on each axial slice to the nearest 1.0 mm, is used as the Z co-ordinate. The CT imaging plane must be parallel to the XY plane and it is absolutely imperative that the gantry of the scanner not be tilted.

As will be discussed later, slice width is an important contributor to accuracy and this varies depending on the technical specifications of the scanner. When this project commenced, the minimum slice width was 2.0 mm, but most scanners now can obtain images at 1.0 mm and less.

All Groote Schuur patients (effectively all the adults in this study) were scanned on the CT scanner in the Radiotherapy department, manufactured by Picker (Model No. 174203). This will be referred to as the GSH scanner; there were several reasons for using this particular scanner:

- This was the scanner used to develop the radiosurgery system; hence the biomedical engineers were familiar with the set-up (and the radiographers were accustomed to the biomedical engineers!)

- At the time, this was the most accurate scanner in the hospital. The two scanners in the Radiology department were not only rather antiquated, but also in constant use for all emergency and elective clinical work and totally over-loaded; hence any research activity was out of the question.

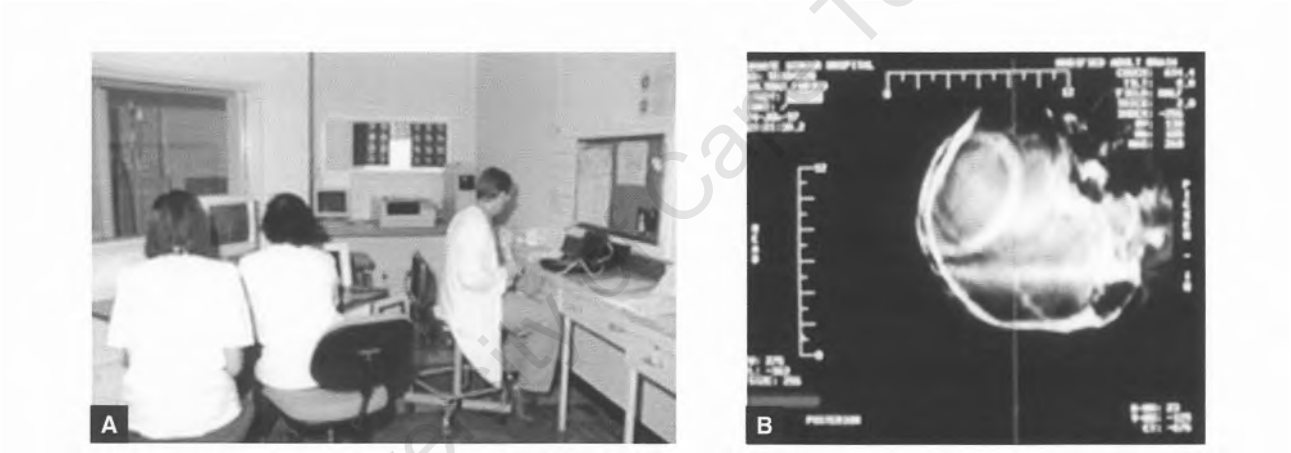


Figure 3.6: The CT control room for the GSH scanner; two radiographers are seated at the scanner console while Dr Allan Taylor enters the stereotactic co-ordinates into the laptop computer (a). A typical CT surview from this scanner; the level at which the scan was taken is demonstrated by the red line and the numerical value for the table position is shown at the top right corner of the screen (b).

CT technology has evolved very rapidly and patients scanned at Red Cross Children's Hospital were scanned on two different scanners (Figure 3.5) with vastly different technical capabilities:

- From 1994 to 1998, an Elscint model 2400 was used (RXH1)
- From 1998 to 2000, a General Electric ProSpeed S, an early model helical scanner was used (RXH2)

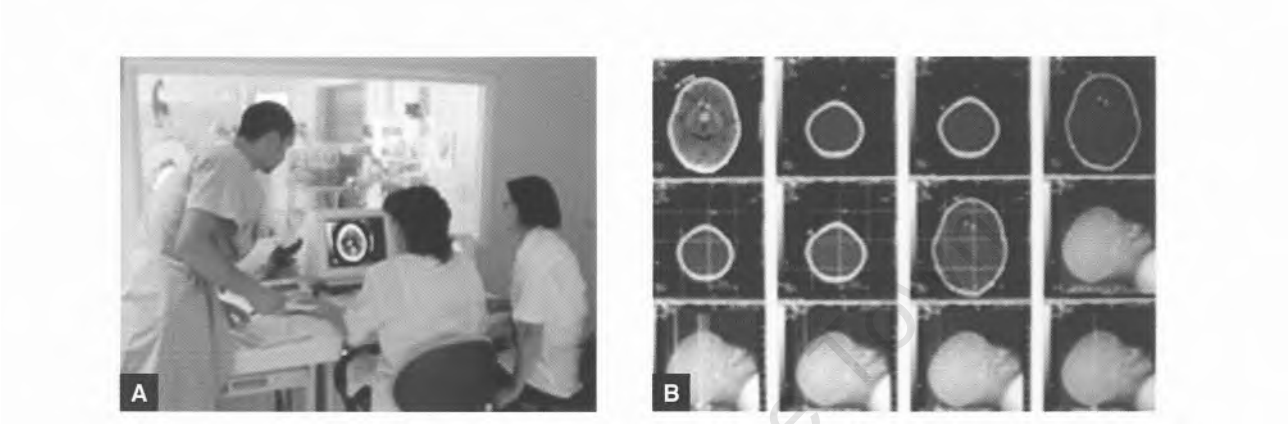


Figure 3.7: The CT control room for the RXH scanner; two radiographers are seated at the scanner console while Dr Tony Figaji selects the appropriate image (a). A series of images from this scanner showing the axial slices and the relevant surviews; the level at which each scan was taken is demonstrated by a line while the numerical value for the table position, and each X- and Y- co-ordinate for the selected target on the axial slices, is shown at the top right corner of the screen (b).

Before doing a clinical case at Red Cross Children's Hospital, a trial phantom was scanned using the Elscint scanner and the data obtained was quite clearly incorrect. Further investigation revealed that manufacturers of the early scanners used either "right hand" or "left hand" configurations for their Cartesian co-ordinate systems as this was not standardized, and the GSH and RXH scanners were different in this respect. The software was therefore re-written to enable the CTSP to function independently of the type of CT scanner used.

3.6.2 Fiducials: from donuts to halo

Stainless steel ball bearings make an ideal fiducial as they are easily visible to the human eye but also highly radiopaque hence can be identified readily on an X-ray or CT scan. Ball bearings served as the fiducials throughout this project, and the first method used was direct application onto the scalp using donut-shaped adhesive discs 18 mm in diameter with a small central perforation, just large enough to hold the 2mm ball bearing snugly.

The first step was to decide where the optimal site for the burr-hole was; this was considered the "entry point". There were two reasons for doing this:

a. the safest and simplest trajectory to the intracranial target must be planned, based on an intuitive understanding of the location of the lesion.

b. the initial planning software generated a printed "setting diagram", the first version of which was absolutely dependent on having a defined "entry point".

Once the burr-hole site had been selected, this "entry point" was marked with a disc containing a ball bearing. The setting jig, a three-legged template conforming exactly to the dimensions of the three legs of the tripod stool which would be used for the surgical procedure, was then placed against the scalp and a small patch of hair shaved in the region of the footpoint of each leg to facilitate attachment of the disc to the scalp. The undersurface of each disc was sprayed with Dow Corning Medical Adhesive B ™, an aerosol silicone adhesive, before being applied with firm pressure and then numbered to facilitate later identification.

Once the discs were securely attached, the ball bearings were inserted into the perforation. Attachment of the discs had to be done with great care as misplacement or dislodgement of even a single disc or its ball bearing would render the whole exercise void and one would have to start again, but remarkably this never occurred. The patient was then taken to the CT scanner and positioned with the array of three discs uppermost. A typical arrangement is seen in Figure 3.8 with a patient who was to undergo biopsy of a left temporal mass.

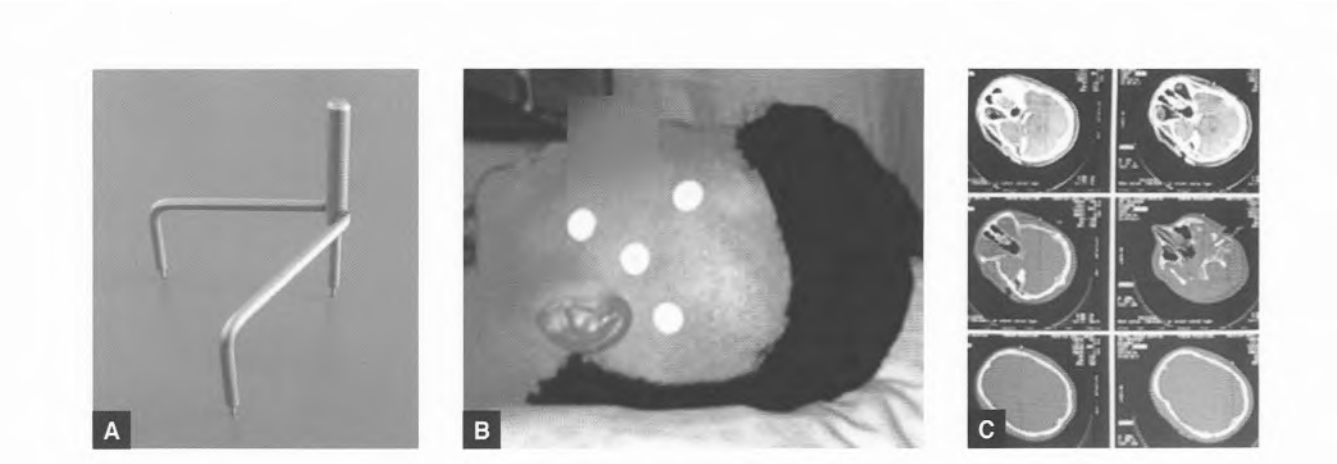


Figure 3.8: Scalp-mounted ball bearings as fiducials. The setting jig (a) and **the** patient with 4 fiducials attached, one for each of the 3 legs and a central fiducial indicating the proposed entry point (b). This patient had a larger area shaved as a craniotomy was planned should the smear have disclosed a high grade tumour. Stereotactic CT scan showing the selected intracranial target (top left image) and the 4 fiducials (lower 4 images) (c).

Upon completion of the scan, the ball bearing was removed as the three vacated perforations then served as receptacles for the three feet of the tripod stool. Care had to be taken not to dissolve the adhesive when prepping the scalp with chlorhexidine/ alcohol; once this had dried, a sterile adhesive plastic drape was placed over the surgical site.

An alternative strategy was to remove the ball bearings and mark the central holes of each of the three discs with an indelible pen, after which they were peeled away. The legs would then be placed directly onto these marks and held in position by an assistant during the surgical procedure, but this was considered much less reliable.

This system of adhesive discs was used for 30 patients and although no case had to be terminated because of a problem related to this system, it was not very robust and one was always concerned that one of the discs might come adrift.

One solution was to place sharp tacks into the outer layer of the skull; the head of each tack served as the fiducial (Figure 3.9) and the concave upper surface served as a receptacle for the footpoint of the tripod. There are some ideas that you only try once; although a compact tapper was manufactured to facilitate controlled placement, it was extremely unappealing to be knocking tacks into a patient's head. Another idea was needed.

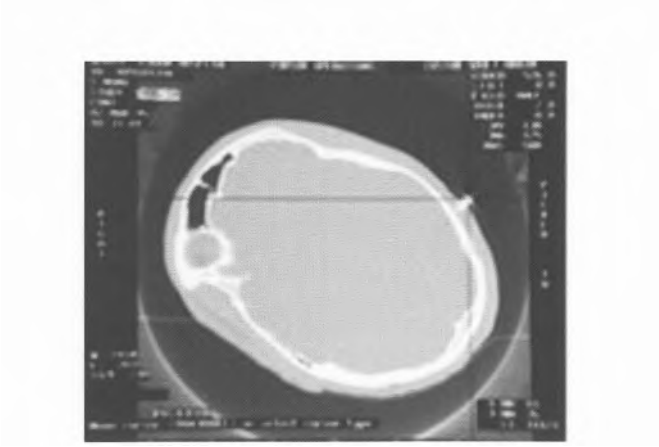


Figure 3.9: Tacks as fiducials. Stereotactic CT scan showing a tack serving as the fiducial, with the head of the tack serving as the centroid.

The solution was very elegant indeed: Dr Allan Taylor suggested that the fiducials be implanted into a halo, which could be secured onto the patient's head. This had the added advantage of serving as a stable platform onto which the tripod stool could be mounted. A lightweight halo was manufactured out of polycarbonate, which was transparent, making the three ball bearings contained inside easily visible. Although the ball bearings were no longer positioned exactly where the feet of the stool were, they continued to be referred to as "leg 1", "leg 2" and "leg 3". The halo was 10 cm in diameter and was able to sit securely on the convexity of the skull, but the only problem was- how to attach the halo to the scalp?

There were two options- either scalp or cranial fixation. Cranial fixation with self-tapping screws placed in the outer table of the skull did however provide secure fixation (Figure 3.10) and this was used in eight patients. Stainless steel surgical screws 2 mm in diameter were sourced and a hand-held power tool used to drill the hole in the skull. A depth stop was used to prevent plunging and the screw was securely inserted using the power tool. Two screws didn't provide any greater stability than one as there was still the possibility of the halo rocking unless it was fixed at three points or more.

The halo was affixed to the scalp with adhesive medical tape for five cases; but this was bulky and wasn't considered reliable enough. A hybrid system was also tried, where one screw was inserted and tape was used to secure the halo at two or three other points.

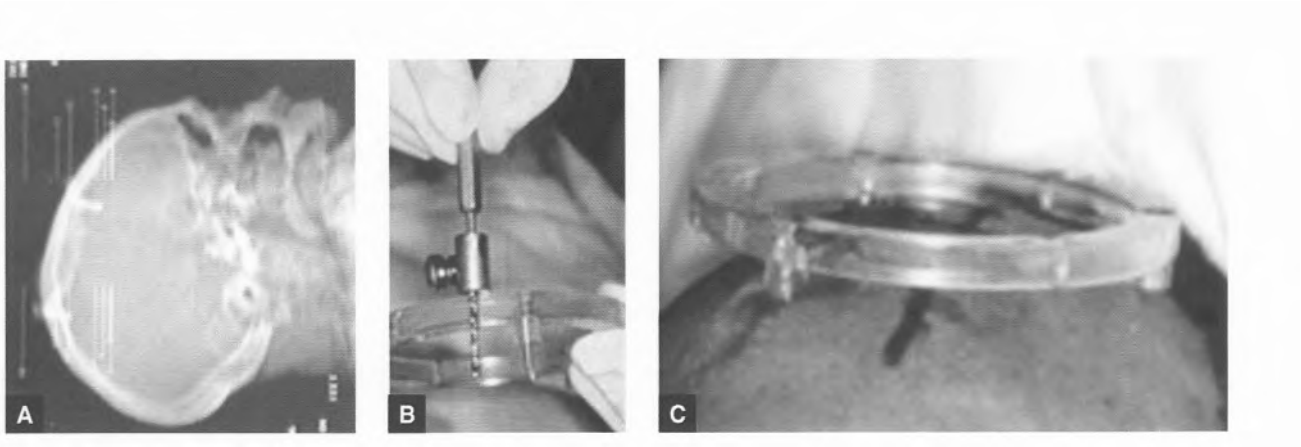


Figure 3.10: Skull-mounted halo, attached with screws. CT surview showing the halo secured with two screws (a); these had been placed using a hand-held power tool with a depth stop to prevent plunging (b). Insertion of the screws resulted in secure cranial fixation of the halo (c).

When the solution finally occurred to us, it was somewhat embarrassing that as surgeons we hadn't thought of it earlier- sutures! In adults the halo was almost invariably applied in the ward; after prepping the scalp and infiltrating local anaesthetic, four or five 2/0 silk sutures provided very stable fixation (Figure 3.11). Younger children were anaesthetized before applying the halo in the Operating Theatre.

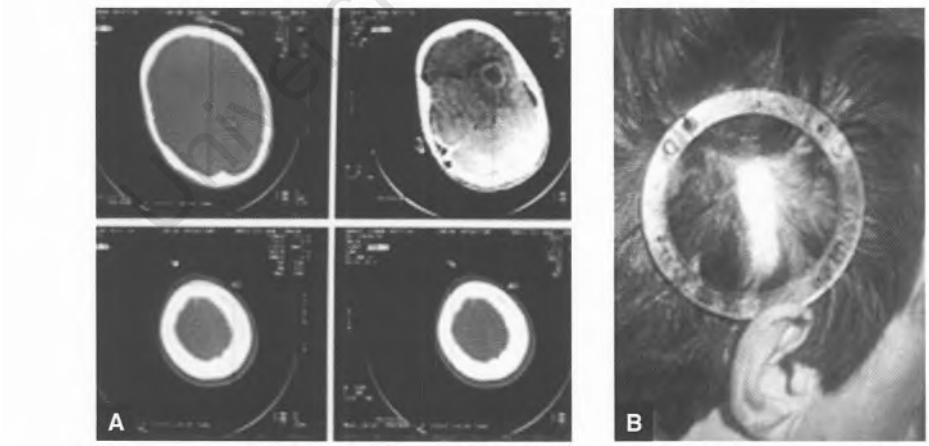


Figure 3.11: Scalp-mounted halo, attached with sutures. CT scan showing the target and the 3 fiducials clearly seen within the halo (a) and a different patient with the halo sutured in place and a small patch of hair shaved for surgery (b).

The prototype halo was manufactured from polycarbonate and therefore could not be autoclaved. After each case, the halo was cleaned and gas sterilized so that it was sterile at the time of attachment to the next patient. Although the exact orientation of the fiducials was not of any importance, as a convention the halo was always positioned with "leg 2" closest to the midline, in order to facilitate identification on the CT scan.

If one considers the different strategies for mounting the fiducials, the development of the project went through three sequential phases, with a fourth phase entered when the production system was introduced:

Phase 1 scalp-mounted adhesive fiducials, with different strategies to prevent loss of these

Phase 2 fiducials housed in the prototype halo

- skull-mounted with one or two screws
- scalp-mounted with adhesive tape
- hybrid fixation (one screw and tape)

Phase 3 fiducials housed in the prototype halo, scalp-mounted with sutures.

This sequence is depicted graphically in Figure 3.12.

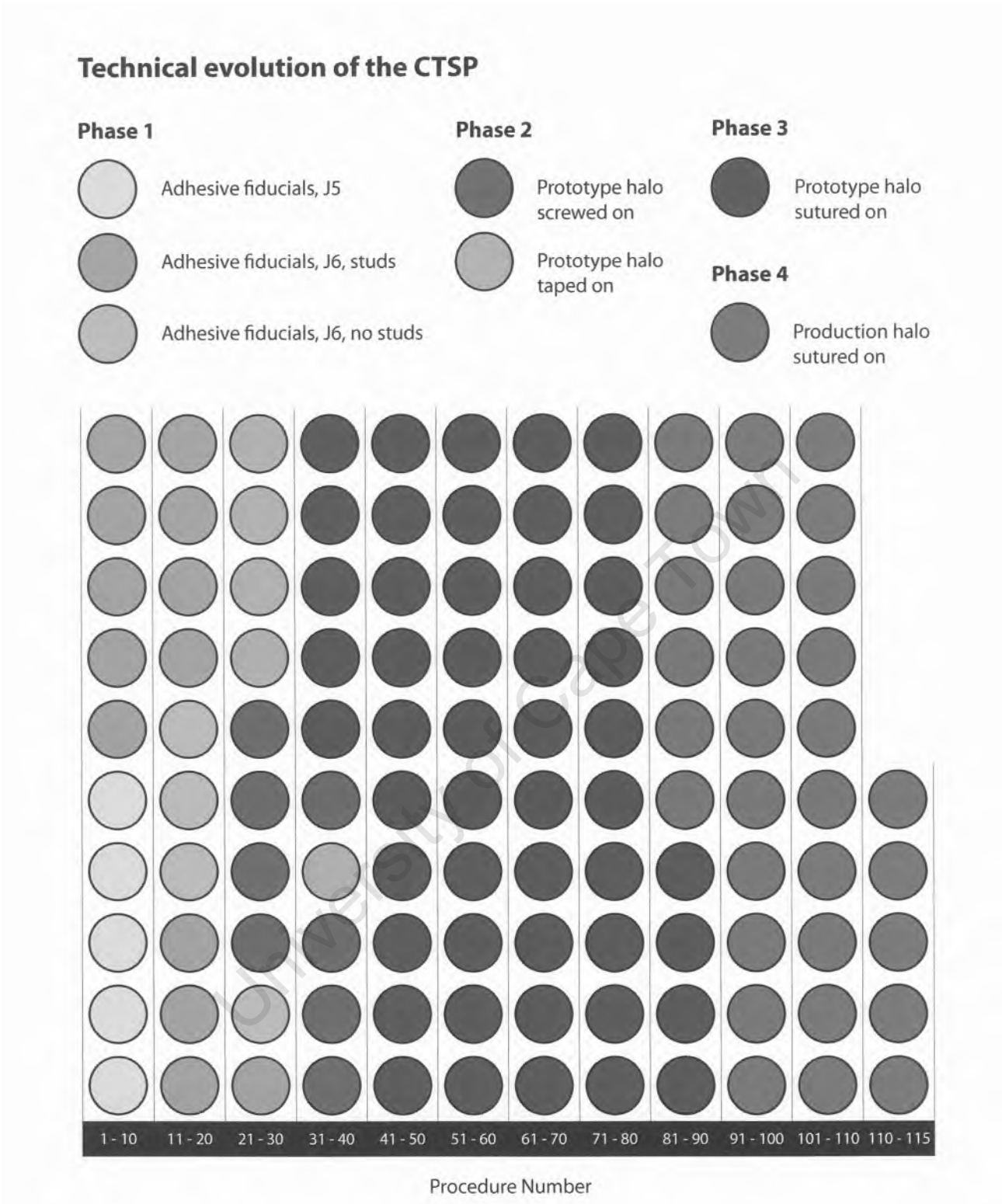


Figure 3.12: Fiducials used for the 115 cases

Phase 1: adhesive fiducials

Phase 2: prototype halo skull-mounted with screws scalp-mounted with tape

Phase 3: prototype halo, scalp-mounted with sutures

Phase 4: production halo, scalp-mounted with sutures

3.6.3 A surgical guidance device: The Tripod

This is the effector of the system and served as the interface between the surgeon with a tool such as a biopsy needle and the patient with a lesion.

As described in Chapter 3.5, the device comprised the following (Figure 3.13):

- A base with *three feet,* the tips of which defined a lower or distal plane
- An *upright post* which had an aperture through which slides a *radial arm,* rotation of which defined an upper or proximal plane; this radial arm could be locked firmly in place by a nut mounted at the top of the post
- A *swivel head* attached to the end of the radial arm via a ball-and-socket connection; this contained a hollow instrument guidance cannula which could be locked firmly in position, defining a specified trajectory

Figure 3.13: The prototype tripod Pointer, the J6, with a isosceles triangle configuration to the legs.

The three legs tapered at the tips and these footpoints fitted snugly into three small holes on the upper surface of the halo.

The instrument carrier was calibrated by tightening a ball-and-socket joint. The swivel head comprised two annular plates, which were clamped into position by tightening two screws with an Allen key, one on the upper surface and one on the lower surface. The outer surface of the instrument guidance cannula had a spherical construct, serving as a ball-and-socket joint with the annular plates on either side. This mechanism locked the instrument guidance cannula securely into position, thus determining the trajectory of the instrument used for the operation.

A versatile aspect of the CTSP was that various different diameter instruments could be used through simply changing the guidance cannula in the swivel head as these had differing diameters and lengths to accommodate instruments varying from biopsy needles to shunt catheters.

As the tripod determined the trajectory of the instrument passed into the brain, it was vitally important that this should be set correctly. The first prototype tripod stool that was used clinically was the "J5" which had the three legs arranged as an equilateral triangle. A problem recognized only at the time of surgery in one of the early cases (Case 4) was a trajectory that quite clearly was grossly incorrect, hence the biopsy had to be performed freehand. Upon review of the data later it was apparent that two of the legs had been transposed, but this had not been detected on the setting diagram, due to the fact that the configuration of the legs (and therefore the fiducials) described an *equilateral triangle,* which was aesthetically pleasing but made it possible to position the frame three different ways, two of which would be incorrect.

The solution was to move legs one and three closer together to describe a *isosceles* triangle. The new model was called the "J6" and the problem did not recur.

The setting of the tripod will be described after considering the two different techniques that were used.

3.6.4 Calibration

3.6.4.1 Imaging

As the co-ordinates entered into the program were derived from the CT scan, it was crucial that this was performed correctly.

The patient was positioned comfortably on the CT table, with the head positioned in the standard head holder; no specific holder was required. Ideally the patient was positioned as they would be during surgery, with particular care taken to ensure there was no scalp deformation. Ensuring the patient is comfortable and understands the importance of not moving their head during the scan is very important; applying soft padding between the patient's head and the head holder, together with a strip of masking tape gently applied across the head further reduces the chances of inadvertent movement while scanning.

A decision was made as to whether intravenous contrast was required; if this would facilitate target selection, 50m1 of Omnipaque® was administered by the neurosurgeon. Often it was helpful for the neurosurgeon to gown up and stay in the CT room in order to reassure the patient.

The scanning protocol varied with different scanners over the course of this project, but with the GSH scanner, a surview was first performed, from which a series of 5mm slices was planned through the region where the target was located. The optimal table position was noted, then a series of 2mm scans was done through each of the three or four fiducials, moving the table manually and determining the optimal position with the help of the low-power laser mounted in the gantry. The sequence followed was to scan from caudal to rostral, scan at the selected table position for the target and then re- scan the first fiducial in order to establish that the head position had not changed during the scan.

The screen cursor was then activated and the X- and Y-co ordinates of each of the 3 fiducials were obtained. This was a crucial step as great care had to be taken to select the image on which the fiducial was seen best and the cursor was then positioned at the centroid of the fiducial. Following this, the images showing the lesion were carefully inspected to select the optimal target and a second intracranial target was often chosen as well. All these X- and Y-values were recorded together with the table position as the Z-co ordinate and the slice number. A pro forma designed by Dr Taylor facilitated data logging and this is shown in Appendix III.

The x, y and z co-ordinates of the three fiducials and the intracranial target are then entered into the laptop computer, using the software specially written for this purpose. This is a critical step as an error in entering this data will have disastrous consequences. An optimal routine is to have two people doing this- one reading out the values while the second enters them, and then these must be checked before proceeding, as is required by Law for Land Surveyors [van Geems]!

Two different techniques were used to set the pointer. The first entailed generation of a printed setting diagram, and the second utilized a simple three-dimensional phantom. Whichever technique was used, the program was run immediately so that the data could be checked and the trajectory ascertained to ensure it was intuitively correct prior to the patient leaving the CT scanner, as the patient would need to be scanned again should either of these appear to be incorrect.

3.6.4.2 The software

The software embodied the three-dimensional mathematical transformations of the co-ordinate system of the CT scanner into the control system of the Pointer. A mouse driven menu ran the various programs written in Turbo C while all other programs were written in True Basic [van Geems], installed on a Compaq Contura/ Aero 4/25 laptop computer. As the biomedical engineers working on the project also wrote the software, this was updated and amended immediately a problem was recognized and this really facilitated the goal of making this interface neurosurgeon-friendly. A "user guide" was written by Professor Adams to facilitate day-to-day troubleshooting; this took the neurosurgeon through the menu which offered four programs:

1. CT Scan input
2. Stool plot
3. Recalculate entry point- on curved surface
4. Recalculate entry point- on plane

1. CT Scan input The x, y and z co-ordinates obtained from the scanner were entered in the order: target, entry point, leg 1, leg 2, leg 3 and "played back" as X, Y and Z. If correct, [Y] (yes) was entered and the program returned to the menu.
2. Stool plot A sequence of simple instructions generated a "setting plot" on the screen; if this was suitable [PRINT SCREEN] was entered and the setting diagram printed (as below).
3. Recalculating the entry point on a curved surface This program was to be used in the operating room if it was necessary to select a new entry point during surgery.
4. Recalculating the entry point on the plane This procedure would be undertaken in the CT scanner.

The software contained a vitally important accuracy check at this point, the "test of transformation precision". Because the fiducials are mounted in a halo and therefore always the same distance apart, it was a simple matter for the program to compute these distances from the co-ordinates obtained from the CT scan and check how closely these matched the known distances.

As will be discussed later, the CTSP program provided with each system contained this calibration data (which is identical for every halo as they are all manufactured in exactly the same way) as well as a second unique set of data which relate to the exact measurements of the phantom and tripod provided with that particular system. It is absolutely essential that the correct data set is used - the consequences of using the wrong phantom calibration data will be clearly apparent

later.

A number of modifications were made subsequently. One of the situations that had to be dealt with was when the selected entry point proved unsuitable at the time of surgery. A method was devised that allowed the neurosurgeon to select a new entry point and then generate a new setting diagram. In order to do this, the following sequence was followed [van Geems]:

1. The tripod was set at 90° using the T-shaped perpendicular setting tool which was removed after fastening the ball-and-socket joint and the tripod is then placed in the surgical field with the feet located in the adhesive discs surrounding the new burr hole.
2. A probe was then passed through the instrument channel and the arm adjusted such that the tip of this probe lay at the midpoint of the new burrhole. A depth stop is fastened on the probe at the point where it exits the top of the instrument channel, allowing one to measure the exact distance the burr hole lies below the tripod.
3. The tripod is then placed on the previously printed setting diagram and a probe used to mark the position of the burr hole on the setting diagram.
4. The distances from the new burr hole to each of the three legs were easily measured
5. These four measurements (distances of the burr hole from the 3 legs and the distance from the top of the tripod instrument channel) were entered into the program and a new setting diagram could be generated in Theatre.

3.6.4.3 The setting diagram

The printed diagram used to set the pointer was the projection of the three footpoints and the points where the vector intersected the proximal and distal planes onto a 2D plane. This setting diagram displayed 6 points, with the option of a 7th:

- One for each leg, labeled "leg1, "leg 2" and "leg 3"
- One labeled **"P"** (proximal)
- One labeled "D" (distal)
- One labeled "T" (target)
- One labeled "E" (entry point) (optional)

A Canon Bubble Jet printer BJ-10SX was used to print the setting diagram. In order to ensure that the printout was exactly to scale, scaling parameters for the X- and Y- co-ordinates were used, but this is probably not required with printers today.

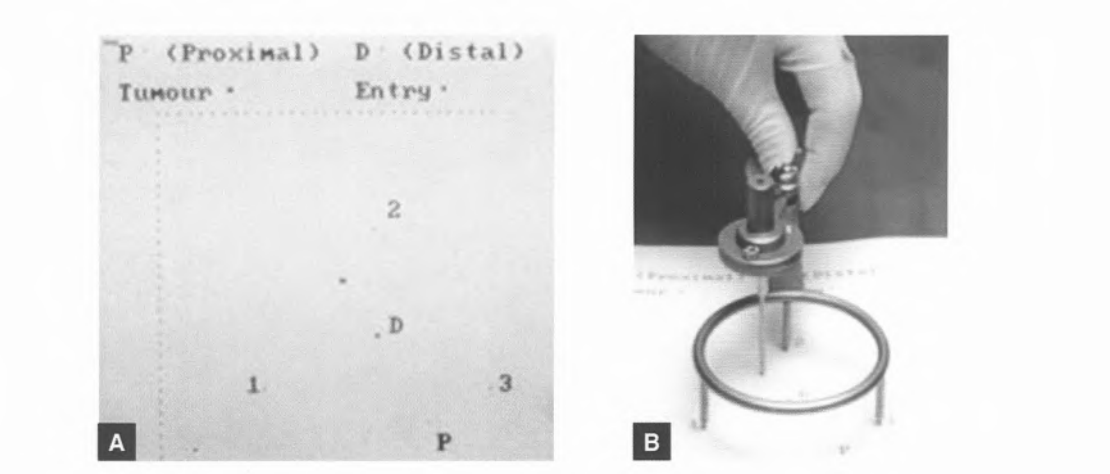


Figure 3.14: (a) The setting diagram represents the vector passing from the intracranial target, T, and continuing to intersect first with the lower plane (described by the three feet of the tripod) at D, and then with the upper plane (described by the swivel arm) at P. (b) The tripod may be set perpendicular if for example, should one require an orthogonal trajectory to define the intracranial target or the entry point, by using the T-shaped perpendicular pointer.

To set the tripod using this diagram one first needed to ensure that the 3 nuts had been loosened i.e. the nut which locked the sliding radial arm in place and the nuts on the superior and inferior plates of the ball and socket joint which locked the swivel head in place.

Setting the tripod with the setting diagram required 4 simple steps:

1. The setting diagram was placed on a flat surface and the pointer positioned such that each of the three legs was on the appropriate point, using the best optimum fit. As mentioned previously, the configuration was changed from an equilateral triangle to an isosceles triangle to eliminate the likelihood of mispositioning the pointer.

2. The second task was to align the instrument channel of the swivel head directly above point P, i.e. the projection of the point where the vector intersects the proximal plane. This was done by first inserting the T-shaped perpendicular setting tool in the instrument channel, which kept the swivel head at 90°, and then tightening the ball and socket joint clamp. The most efficient procedure was to tighten the inferior nut "finger-tight" and then use the Allen key to tighten the superior nut. The nut securing the radial arm where it traversed the vertical post was locked once the instrument carrier was in the correct position, directly coincident with P.

3. The third task was to define the vector from point **P** to point **D** (i.e. where it intersected with the lower plane). This was done by loosening the nut on the superior plate of the ball and socket joint, inserting a long straight stainless steel probe through the instrument channel in the swivel head and then gently angling this until the tip rested exactly on point **D;** the swivel head was now locked in position by again tightening the superior nut.

   At this point, the trajectory of the tripod should clearly be in the direction of the intracranial target.

4. The final task is to calibrate the **depth** to which the cannula was to be inserted into the brain. The distance from the top of the instrument carrier to the intracranial target was given on the printout and this was then set on the cannula by measuring this distance from the tip with a ruler and then sliding a depth guide along the shaft, gently locking it in place at the measured distance. Care had to be exercised in doing this as tightening the screw too much would permanently damage it, leaving an indentation.

Figure 315: **A** depth stop is applied to the biopsy needle with gentle pressure after measuring the required depth with a ruler.

The tripod was now placed on the patient's head and the trajectory checked to ensure that it was intuitively correct. This was an absolutely vital step as the software was able to detect errors in the co-ordinates of the fiducials but was not able to detect an error in the target co-ordinates. A three dimensional phantom was designed as an extra check prior to surgery, but to the neurosurgeons it seemed that this was a much easier method of setting the tripod and ultimately this became the method of first choice.

3.6.4.4 The 3D phantom

The setting diagram presented a number of challenges. It was quite a fiddle to set the pointer accurately and in order to do so in the operating theatre, the printout had to be placed under a sterile sheet of transparent plastic as it wasn't sterile. This printout did in fact serve as a permanent record, which was useful for documentation.

As the central concept was to replicate the three-dimensional space of the patient in order to set the trajectory on the pointer, it was suggested that this could be done using a three-dimensional phantom. The initial idea was to use this as a back up to check the trajectory determined by the setting diagram, but as it was so simple to use the phantom, this soon became the preferred technique.

The 3D phantom was made out of stainless steel and was therefore autoclavable. It consisted of a flat surface containing three small holes corresponding to the legs of the pointer. The top surface had a large opening and was mounted on four posts; one of these had a millimeter ruler which served as the z-axis. The axis running parallel to the anterior aspect of the base (in the corona) plane) was the x- axis and the y-axis was on the same axial plane but ran from front to back (in the sagittal plane); each of these axes also had a stainless steel millimeter ruler.

A metal block served as the intracranial target with a 1mm wide hole on the upper surface giving the exact location of the target. After calibrating the phantom for the z co-ordinate (depth below the platform) and the x co-ordinate, the procedure was completed by sliding the target block along the y-axis to the calculated co-ordinate value.

The software had needed to be modified to give the x, y and z values for the intracranial target so that they could be set directly on the phantom. Each is set in turn by moving the marker shown in Figure 3.16 to the specified position and then tightening the screw to lock each co-ordinate in place.

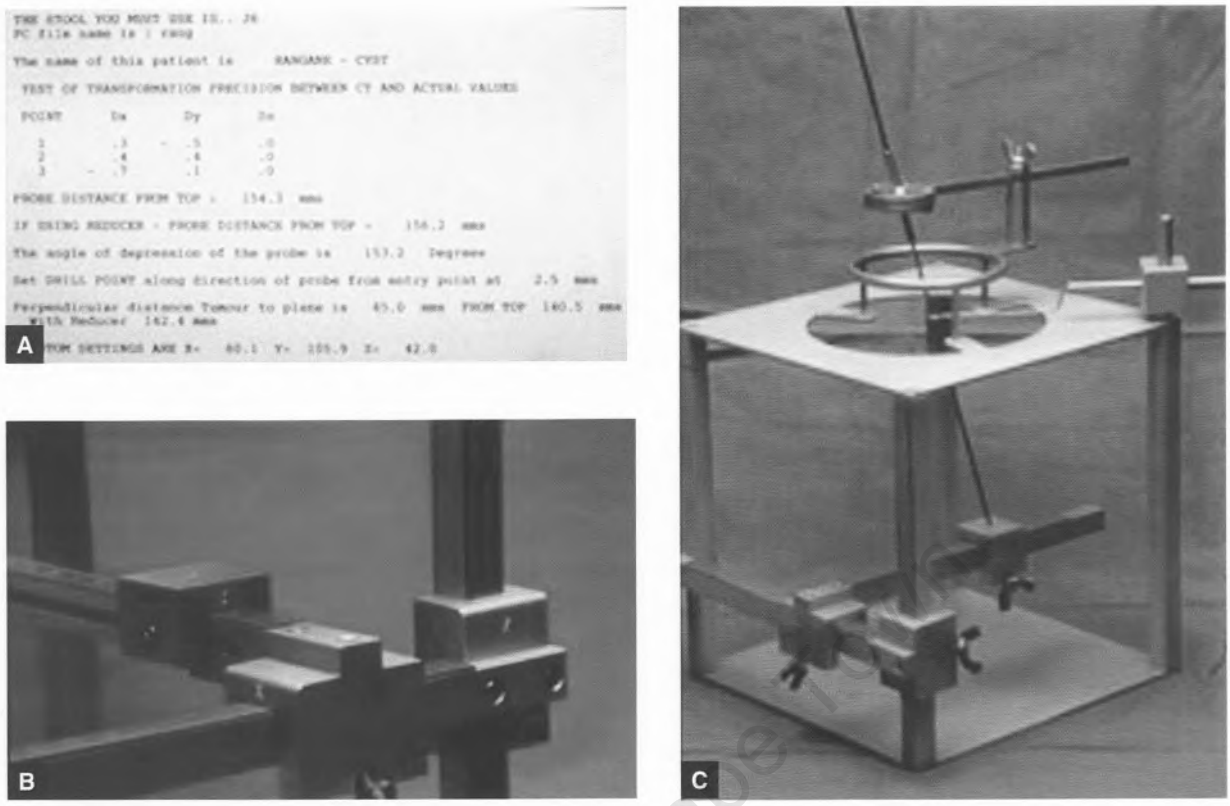


Figure 3.16: The printout giving readings for x-, y- and z- coordinates (a) to be set on each of the axes of the 3D phantom (b); the prototype 3D **phantom with the tripod** set such that the instrument passes through the burr hole indicator (c).

The tripod was then mounted on the platform with a long straight stainless steel pointer running through the instrument carrier and resting in the target hole. The nut atop the vertical post was tightened first, locking the sliding arm in place and then the swivel head was locked, securely setting the trajectory.

One limitation of this arrangement was that the trajectory to the intracranial target had to pass through the gap in the centre of the platform. This in fact was an advantage in real terms as it avoided having a trajectory which was particularly angled and therefore more likely to be inaccurate.

If the burr hole is not centered or the trajectory is angled, the position of the burr hole could be replicated on the phantom using a small circular loop at the tip of an adjustable arm mounted on the phantom. This was easily performed; after completing the burr hole, the swivel head was set at 90° as described earlier and the tripod mounted on the halo. The steel probe was passed down the instrument channel until it reached the burr hole and then calibrated by tightening the

depth stop. With the tripod then mounted on the phantom, the tip of the steel probe marks the position of the burr hole. The small circular burr hole indicator is then positioned at the tip of the probe and the trajectory of the tripod adjusted until the probe passes through the burr hole indicator to the target.

It is important to emphasize that the software that accompanies each CTSP system contains a set of calibration data which is unique to each system. This data represents a set of exact measurements made of the tripod and phantom following manufacture; although these are all machined in exactly the same way, there are small individual variations which may adversely affect accuracy should the incorrect data be used. The consequences of this will be apparent later.

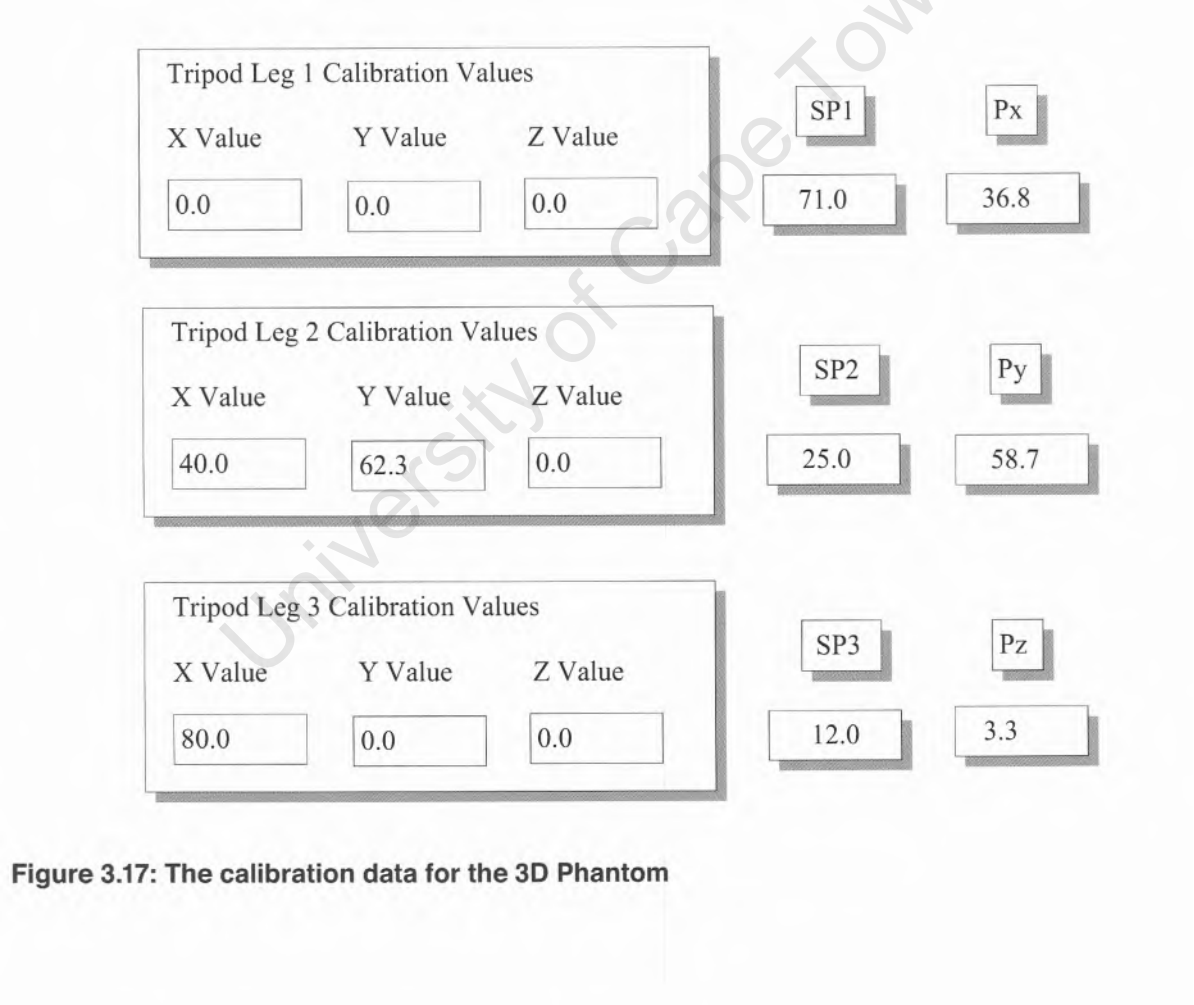


Figure 3.17: The calibration data for the 3D Phantom

This data set is shown in Figure 3.17 and represents the following measurements:

1. The three sets of x-, y- and z- co-ordinates all relate to the halo, with "leg 1" as the datum point. Z.0 for all as the legs are all on the same plane when measured.
2. The next three values relate to the tripod:
   Sp1= the height from the tip of the tripod leg to the centre of the ball in the tripod arm
   Sp2= the proximal length of the biopsy guide tube (from the centre of the ball)
   Sp3= the proximal length of the cutoff guide tube (from the centre of the ball)
3. The last three values relate to the 3D phantom.
4. **Px, Py, Pz =** the zero settings for the phantom when the target block sits directly under leg 1.

3.6.5 The Operation

Once the neurosurgeon was satisfied that the planned trajectory of the tripod looked correct, the patient was taken to the Operating Theatre, or to the ward if there was going to be a delay in starting the case.

There was sufficient time to autoclave the tripod and the various peripherals such as biopsy needles and depth stops, the ruler and the other peripheral instruments and attachments while the anaesthetist took care of the patient. Anticonvulsants and steroids were administered if there was an appropriate indication, and an intravenous dose of an antibiotic was given if the neurosurgeon requested this.

The disc marking the entry point was removed and the scalp was prepped by the neurosurgeon with chlorhexidine and alcohol in the usual fashion with particular care taken to ensure that the other adhesive discs marking the footpoints were not dislodged. Once the halo was introduced this was no longer an issue and the entry point was also no longer specified. A solution containing long acting local anaesthetic and a vasoconstrictor (Marcaine® and Por-8®) was infiltrated with care taken not to do this too close to the fiducials so as not to displace them. The surgical site was then covered with an OpSite® adhesive drape, which was initially applied in the centre and then carefully folded over the rim of the halo, resulting in a very stable arrangement if done correctly.

If the printed setting diagram was to be used to set the tripod, this was placed on the surface of a table and covered with an OpSite® adhesive drape. Once the 3D Phantom was introduced, this was no longer required as the phantom was autoclaved (Figure 3.18). It was always necessary to re-set the tripod prior to surgery as all the clamps were loosened prior to autoclaving to prevent damage due to the high temperatures.

The scalp incision was usually made in the centre of the halo and the edges held apart with a small self-retaining retractor. The pericranium was gently scraped aside and the Hudson Brace used to drill a 12 mm diameter burr hole. Prior to incising the dura, the tripod was set and positioned to ascertain the trajectory; on rare occasions it was necessary to nibble the edge of the burr hole with a Leksell rongeur if the trajectory was quite oblique. At this point the instrument to be passed into the brain was also checked; if a biopsy was to be taken, the depth to which the needle would be inserted was set by applying a depth stop to the shaft. The depth stop was typically placed 5-10 mm short of the calculated depth as biopsy would not be taken from the tip of the needle, but 5-10 mm proximal to the tip and this therefore needed to straddle the target. Once the neurosurgeon was satisfied that the procedure could be performed, the dura was incised, a small opening made in the pia with bipolar electrocautery and the procedure performed Figure 3.18). Various different biopsy needles were used, as will be discussed in Chapter 6; techniques for placing catheters in cysts, aspirating abscesses and performing stereotactic craniotomies will be described elsewhere.

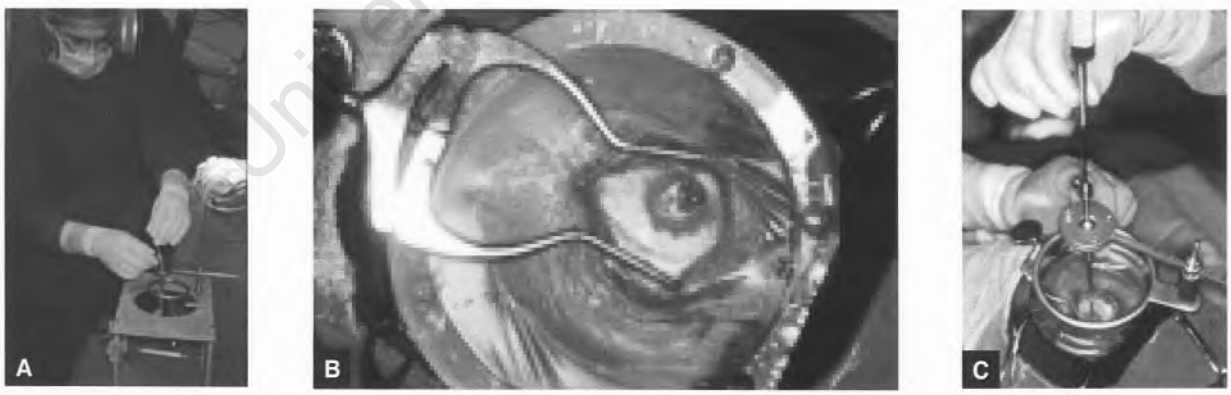


Figure 3.18: Surgery. The trajectory of the tripod is checked in the Operating Theatre prior to performing the biopsy (a). The self-retaining retractor must be carefully positioned so as not to displace the halo (b); the tripod is coupled to the halo and biopsy is taken by aspirating gently before closing the window of the side-cutting needle (c).

3.7 Perspective

The CTSP developed out of close collaboration between biomedical engineers and neurosurgeons, with important input from colleagues including radiologists and radiographers as well as theatre nurses. This process transformed a conceptually novel but unwieldy prototype into a potentially useful neurosurgical device; the main features of this were the four sequential phases for securing the fiducials, and the introduction of the 3D phantom.

The CTSP was well tolerated by patients as the halo was so small and light. The drawbacks of a heavy conventional stereotactic frame have long been recognized [Austin]; a recent contribution described the use of a lightweight customized (and presumably rather costly) miniature stereotactic platform which also had a tripod configuration and was attached to three skull-implanted fiducials [Fitzpatrick].

Furthermore, the four sequential steps for using the system were intuitive and simple, making the CTSP attractive to busy neurosurgeons who were not specialists in the field of stereotaxis.

As accuracy was the most essential determinant of whether this system would be clinically effective, this was rigorously evaluated in the laboratory prior to clinical application. This laboratory accuracy data was an important component of Dr van Geems doctoral thesis, but the salient findings will be summarized in the next chapter as this was critical in laying the foundation for the ongoing clinical use of the CTSP, and this data may not be readily available to the reader.

Chapter 4

Accuracy and Precision

4.1 Introduction

"The purpose of incorporating stereotactic methodology into neurosurgical operations is to achieve a consistently high degree of accuracy in localizing intracranial targets" [Maciunas 1994]. In view of this, the first question any neurosurgeon will ask when looking at a stereotactic system is "What is the accuracy?"

In a landmark series of experiments at Vanderbilt University, Maciunias and Galloway rigorously asked this question of four of the most commonly used stereotactic systems, having unambiguously defined the appropriate terminology [Galloway 1991, Maciunas 1991, Maciunas 1994];

- **Accuracy** refers to the ability of the system to provide the true location of a point in space; this encompasses both unbiasedness and precision
- A series of observations that have a minimum of spatial error and tend to the true value are without skew or **"unbiased"**
- **Precision** reflects the variability of the system in repeatedly localizing the same point in space Le. reproducibility or ability to return to the same location.

A system can be precise but still inaccurate if there is a large degree of bias in its measurements [Benardete_2001].

Manufacturers readily claim sub-millimetric accuracy but what they are referring to is the mechanical accuracy of the device; published performance specifications for stereotactic devices call for submillimetric mechanical accuracy [Galloway 1991]. In manufacturing the production version of the CTSP, the machinist has to be within tolerances in the order of 0.05- 0.10 mm [Mundell PJ, personal communication]. Although this is an essential foundation for a clinically reliable stereotactic system, accuracy in practice encompasses a much wider range of factors.

4.2 Application accuracy

While one cannot simulate all the actual operative factors in a laboratory experiment, an attempt should be made to replicate the 'real-life' situation as closely as possible. This has been termed

application performance or application accuracy by the Vanderbilt group [Maciunias 1991, Maciunas_1994].

A multitude of factors may affect the accuracy of a stereotactic system; some will be specific to the particular system used, but some are generic and apply to all stereotactic systems.

One of the more important of these generic factors is the scanning protocol, the impact of which can be readily quantified using a phantom. The role of slice width was clearly shown in a study where a phantom was scanned at slice thickness varying between 5.0 mm and 1.5 mm with interscan spacing varying from 3.0mm to 0.5mm; mean error decreased by 23% as slice width diminished and by 45% as interscan spacing diminished [Bucholz]. At a slice width of 1.0mm, the major stereotactic systems may still have an appreciable error, as shown in Table 4.1 [Maciunas 1994]. As imaging technology has continued to improve, slice width has fallen below 1 mm with contemporary scanners, some of which have a voxel size of around 0.5mm^3.

Measurement (millimeters)	BRW	CRW	Compass	Leksell
Mean	1.9	1.8	1.2	1.7
Standard deviation	1.0	1.1	0.6	1.0
Minimum value	0.1	0.0	0.3	0.2
Maximum value	5.0	4.9	3.2	4.9
95% CI	3.6	3.6	2.2	3.4
99.9% CI	5.0	5.2	3.1	4.8

Table 4.1: The application accuracy of four stereotactic frame systems when using a 1mm slice width CT scan protocol (from Maciunas_1994]). The application accuracy fell markedly with either angulation of the gantry or increasing the slice width.

Less easy to quantify is the accuracy of an actual surgical procedure, although it has been suggested the position of the probe tip could theoretically be localized by radiography [Kitchen 1993]. This group noted that postimaging brain distortion could be due either to physiological or physical factors [Dorward_1998]; physiological factors included manipulation of blood volume, use of diuretics and ventilation, while physical factors encompassed patient positioning, gravity, withdrawal of CSF or other intracerebral tissue. The effect of gravity when changing patient position had been known since the days of air encephalography [Thulin].

An elegant study using MRI demonstrated that changing from supine to prone resulted in a registration error of around 2mm, leading the authors to recommend that patients should ideally be scanned in the same position that will be used for surgery [Rohlfing].

Intraoperative brain shift during stereotactic brain biopsy may be observed utilizing intraoperative MRI and the following classification has been proposed [Bernays]:

1. inward (due to atrophy) or outward (due to raised ICP) shift of the brain surface
2. shifting of the target, particularly with small firm lesions, or those with a firm capsule
3. midline shift occurred following decompression of cystic or necrotic masses

A simpler approach to verifying the intracranial position of the instrument is to implant a silicon sphere which can be detected on the postoperative scan [Alesch]. One way to verify accuracy is by comparison of the preoperative and postoperative scans as there is often a small gas locule or dot of haemorrhage at the biopsy site, but this is difficult to do unless both scans are done in the same fashion, ideally on the same scanner. This was seldom the case in this series, as the stereotactic scan was only done on the same scanner as the preoperative scan in five paediatric biopsies.

4.3 Laboratory testing of the CTSP

As outlined in Chapter 3.6, three different stereotactic methodologies were considered in the evolution of the CTSP. These were the initial Stereophotogrammetric Pointing Device (SPD), followed by the introduction of the tripod with the stereophotogrammetric system for backup, and ultimately the CTSP as a stand-alone device. At each step of this process, laboratory tests were conducted to assess the accuracy of the system and these have all been detailed in Barbara van Geems doctoral thesis [van Geems]. As the data pertaining to the stand-alone CTSP is considered highly relevant to this thesis, the results will be summarized here.

4.3.1 Accuracy of the CT Scanner

As the CT scanner was used as the measuring device for these tests, it was important to first establish how accurate this is. All accuracy tests were performed on the previously described Picker CT scanner (the "GSH scanner") which had a minimum slice thickness of 2.0 mm and a minimum measuring resolution of 1.0 mm on each slice.

It has been pointed out that there is a common misconception that if you have slice thickness N, system accuracy cannot be better than N [Galloway 1991], and van Geems calculated the measuring accuracy for this scanner to be 1.5mm using this protocol [van Geems, p91].

4.3.2 Phantom Head Study

The first experiment to establish application accuracy entailed scanning the black phantom head which had been used for the development of the SPG system (Figure 3.2). This was secured on the CT table and scanned, following which a setting diagram was generated, the tripod calibrated and a needle inserted into the head. Van Geems concluded "from repeated phantom trials, the pointer tip placement was in the range of 2mm" [van Geems, p96].

This experiment was conducted prior to the first clinical applications and although it was reassuring, the phantom only had a single fixed target and a more comprehensive laboratory accuracy test was requested by the neurosurgeons once the halo was introduced.

4.3.3 Ring Phantom Study

A test phantom was designed with a polycarbonate halo identical to the prototype used clinically; this was rigidly mounted on three posts, above a platform which contained narrow twelve plastic posts of different heights, each of which had a 2 mm ball bearing mounted on its summit (Figure 4.1). These targets were therefore distributed over a wide volume of "intracranial" space.

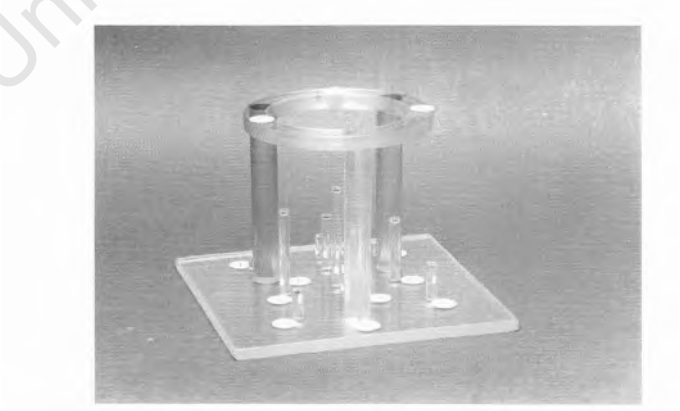


Figure 4.1: The ring phantom

An "error free" set of 3D co-ordinates for the 3 fiducials and the 12 targets could be obtained using the reflex microscope which, as previously mentioned, has a measuring precision of 4 micrometers in all three axes.

Van Geems describes the approach as follows: "Using the three leg markers as the common points between the CT scan system and reflex microscope system, the 3D coordinates of the 12 lesion markers were transformed into the reflex microscope system, using the Rodrigues transformation" [van Geems, p97].

These results are shown in table 4.1, and show the accuracy of the measuring system alone, prior to testing the CTSP.

Marker	**Difference in X (mm)**	**Difference in Y (mm)**	**Difference in Z (mm)**	**Vector difference (mm)**
Fiducial 1	-0.7	-0.0	-0.3	0.7
Fiducial 2	+0.2	**+0.0**	+0.3	0.4
Fiducial 3	+0.5	+0.0	+0.0	0.5
		Mean vector difference		
				0.5
		Standard deviations		
	0.6	**0.0**	**0.3**	**0.2**
Target 1	**-1.5**	-1.4	-0.8	2.2
Target 2	-0.1	-0.3	-1.1	**1.1**
Target 3	+0.1	-0.7	-1.2	1.4
Target 4	-0.4	-0.9	-0.6	1.2
Target 5	+0.1	-1.3	-0.7	1.5
Target 6	**+0.1**	-1.0	-0.5	1.1
Target 7	+0.1	-0.9	-0.4	1.0
Target 8	-0.2	-0.9	-0.6	1.1
Target 9	-0.7	-1.6	-0.6	1.9
Target 10	-1.1	-0.2	-0.2	1.1
Target 11	+0.0	+0.2	-1.1	1.1
Target 12	-0.3	-1.6	-0.7	1.8
		Mean values		
	-0.3	**-0.9**	-0.7	1.4
		Standard deviations		
	0.5	**0.6**	**0.3**	**0.4**

Table 4.1: Precisions for the Rodrigues transformations for the three fiducials and the twelve targets **in the ring phantom** [from van Geems, p 97 and 98].

The X-, Y- and Z- coordinates for each target point were then entered into the computer and a setting diagram produced for each target. The tripod was calibrated for each of these points and coupled with the halo atop the ring phantom and a probe passed to the calculated depth. A small blob of putty had been placed on top of each target and the exact position of the tip was established by the indentation made in the putty. After this had been done for 11 of the targets (the 12th could not be reached as it was behind a pillar), the phantom was examined in the reflex microscope; the results are shown in Table 4.2 with the vector difference being the actual distance between each target and the corresponding indentation. Van Geems highlighted the fact that the mean values were similar to those found in the previous experiment (table 4.1), but the standard deviations were larger. She concluded: "...the overall accuracy decreases from a mean of 1.3 and a standard deviation of 0.4, to a mean of 1.8mm with a standard deviation of 0.3mm" [van Geems, p 99].

Marker	Difference in X (mm)	Difference in Y (mm)	Difference in Z (mm)	Vector difference (mm)
Target 1	+0.8	-0.2	-1.7	1.9
Target 2	-0.7	+0.2	-1.6	1.7
Target 3	-0.4	+0.7	-0.8	1.2
Target 4	-0.9	+0.7	_0.6	1.3
Target 5	_0.8	-1.7	-0.3	1.9
Target 6	+1.2	-1.2	-0.5	1.7
Target 7	-0.2	-0.8	-1.0	1.4
Target 8	+0.1	-2.2	-1.8	2.8
Target 9	-0.6	-1.3	-1.3	2.0
Target 10	-0.4	-1.5	-0.0	1.6
Target 11	-0.6	+0.3	-2.3	2.3
		Mean values		
	-0.2	-0.6	-1.1	1.8
		Standard deviations		
	0.7	1.1	1.5	0.3

Table 4.2: Differences between the actual position of each target and the tip of the tripod, set for each target after generating a setting diagram [from van Geems, p 99].

Once the 3D phantom had been introduced into clinical practice as a back-up to calibrating the tripod using the setting diagram, it became apparent that this could also be used to calibrate the tripod. Prior to introducing this into clinical practice, it was necessary to ascertain the accuracy of this method, using the same protocol used to check the accuracy of the setting diagram method. The data are shown in Table 4.3; van Geems concluded: "the mean vector difference for reaching a lesion marker is 1.9mm, with a standard deviation of 0.6mm, with the greatest vector error of 2.6mm" [van Geems, p116].

Marker	Difference in X (mm)	Difference in Y (mm)	Difference in Z (mm)	Vector difference (mm)
Target 1	-0.6	+0.4	-1.4	1.6
Target 2	+1.0	+0.0	-1.6	1.8
Target 3	+0.9	-0.2	-1.8	2.1
Target 4	+0.7	+0.5	-0.7	1.1
Target 5	+1.0	-0.1	-1.5	1.8
Target 6	+1.5	+0.2	-1.0	1.8
Target 7	+1.0	+0.5	-1.3	1.7
Target 8	+0.9	+0.9	-1.3	1.8
Target 9	+0.7	-0.7	-2.3	2.5
Target 10	+0.4	-1.4	0.9	1.7
Target 11	+1.6	+0.4	-2.0	2.6
		Mean values		
	+0.8	+0.1	-1.4	1.9
		Standard deviations		
	0.6	0.1	0.4	0.6

Table 4.3: Differences between the actual position of each target and the tip of the tripod, set for each target using the 3D phantom [from van Geems, p1161.

These results indicate the accuracy of the CTSP under the best possible circumstances- patient movement during scanning is not a factor and there is no possibility of the halo moving in relation to the targets.

Consideration was given to conducting a study using formalin-fixed heads in the manner as described by others [Dormont, Whittle], but it was felt that this would pose substantial logistic challenges and would add little to the phantom studies described above.

4.4 Specific factors affecting clinical accuracy using the CTSP

As with all stereotactic systems, the neurosurgeon has to be aware of all potential sources of inaccuracy, throughout the procedure. Of course, familiarity leads to facility and the more the system is used, the less likely these avoidable errors will occur.

i. Application of the halo

Patient movement

Patient movement is restricted with conventional stereotactic frames as they are bolted to the scanner table and operating table. This is not without its own problems, as the weight of the head is considerable and its position can shift in relation to frame over the period of time from application, through scanning to surgery [Maciunas_1994 994].

Adams and van Geems' early development of a stereophotogrammetric system to track patient movement has already been described. This technique was considered overly elaborate for point stereotaxis where scanning times were short and patients readily understood the need to lie still and were reminded of this by a single strip of masking tape lightly draped across their head. Very young patients underwent general anaesthesia for attachment of the halo and performance of the CT scan.

Scalp movement

Such skin-surface markers do contain an important potential source of error due to movement of the scalp [Galloway_2001]. This may be normal to the skull surface due to skin swelling (such as following infiltration) or skin drying, or may be tangential due to traction on the scalp from the headrest or drapes.

A number of modern "frameless" stereotactic systems use adhesive fiducials attached to the skin of the face and scalp. The fiducials used here have a fixed relationship with each other as they are housed in the halo, but great care must still be taken to avoid scalp movement. The starting point is to mount the halo securely, ideally over the frontal and parietal eminences where it sits best, and then position the patient appropriately in the scanner and on the operating table.

Trajectory

Selection of halo position in relation to target will determine the trajectory to the lesion. The more orthogonal the trajectory, the better, so one should try to avoid too great an angle to the lesion in

applying the halo. The burr hole (or "entry point") must be within the halo.

ii. CT Scan

Patient movement will be detected by the test of transformation precision, but this will not detect movement of the halo by scalp deformation. It is best to scan the patient with the head in as close a position to that planned for surgery. Usually this will be with the halo uppermost; not only does this diminish traction on the scalp, but also prevents any gravity-induced brain shift from altering the position of the intracranial target.

The role of slice width has already been alluded to and it is vital that the gantry of the scanner NOT be tilted.

When the screen cursor is activated, it is important that the centroid of the fiducial be clearly identified and the most appropriate target selected. Misidentification of fiducials will be detected by the software but wastes time as the data has to be re-entered.

iii. Data entry and calibration of the tripod

It is important to check that the units of table position and on-screen cursor the same. The data should be entered by two people and once data has been entered, this should be checked again.

Calibrating the 3D phantom

The target block must be positioned at the correct X-, Y- and Z-co-ordinates; although the scale is given in millimeters, 0.5 mm increments are feasible.

Setting diagram

Should the setting diagram be used to set the tripod, the 3D phantom can be used to check the trajectory, but one cannot do the reverse, i.e. use the setting diagram to check the 3D phantom-determined trajectory.

Setting the tripod

It is absolutely essential that the sequence described is followed:

1. tighten the nut on top of the post, securing the radial arm as this has a tendency to tilt the long arm upwards and this must be secure before the instrument guide is set
2. tighten the ball and socket joint holding the instrument guide using the Allen key to secure the screw on the upper surface of the two parallel plates (the lower screw having been

"finger-tightened" already).

If done in reverse, there will be a tendency for the radial arm to tilt upwards by 1-2 mm which may be magnified at the tip given the angular setting; this is usually apparent at the time of setting the device, and will always be obvious if the tripod is placed on the 3D phantom as a final check immediately prior to introducing the instrument into the brain.

It is important to remember that even a slight misangulation can translate into a large angular displacement at the tip [Maciunas 2000].

iv. Surgery

The patient must be draped so as not to displace the halo, which is readily secured with steridrape; applying the steridrape in the centre and then gently tucking it over the rim of the halo works best.

The importance of burr hole placement in diminishing the effects of scalp retraction have been mentioned.

Once ready to perform the procedure, the assistant must hold tripod in place carefully without shifting the halo. Meticulous technique is required in setting of depth stop accurately and using the biopsy needle correctly.

As previously discussed, the various intraoperative events that may cause brain shift should be avoided, such as avoiding the ventricle, recognizing tissue displacement and using appropriate anaesthetic techniques.

v. Components

The production version of the CTSP is manufactured to high standards, compliant with the ISO 90 process and although minimal maintenance is required, deformation of any of the instruments will markedly compromise accuracy.

4.5 Perspective

This laboratory study showed a mean vector difference of 1.8mm with a standard deviation of 0.3mm using the setting diagram to set the tripod; using the 3D phantom this decreased marginally to 1.9mm with a standard deviation of 0.6mm, with the greatest vector error of 2.6mm. This level of accuracy was considered sufficient for clinical application.

When considering accuracy in the clinical context, it is helpful to consider Gildenberg's proposal, that one ask "How accurate do I need to be today?" [Gildenberg_2001]. There is clearly a "hierarchy of accuracy" with increasingly elaborate systems [Kitchen 1993], and matching the complexity of the intervention to the problem at hand is sensible. If one is approaching a small lesion in a critical or deep location, the answer to Gildenberg's question is obviously "very accurate", but if one is biopsying a hemispheral tumour, perhaps there is more margin for error.

When using the CTSP, the "test of transformation precision" is an appropriate moment to reflect on this question; often the "error" between the legs will be below 1 mm, but if it is greater than 1 mm, one needs to give consideration to repeating the scan.

The most useful "real world" reflection of application accuracy is an analysis of results in clinical practice, which was a major purpose of this dissertation. One way to frame that question is to ask how often the procedural goal was met, and this will be addressed in the next chapter. Safety, as reflected by the frequency and severity of complications, is another very important issue that can only be determined once a device is used clinically.

Chapter 5

Overview of Procedures performed

5.1 Overview and Methods

Data was prospectively recorded during the development phase of the Cape Pointer from June 1994 until June 1998; this comprised 76 patients who underwent a total of 83 stereotactic operations. The operative logs were subsequently retrospectively reviewed to capture a further 24 patients who underwent stereotactic surgery over the period June 1998 until June 2000, following the installation of the first commercially manufactured Cape Town Stereotactic Pointer. This comprised a further 24 patients who underwent a total of 32 stereotactic operations.

As described in Chapter 3.6.2, the evolution of the CTSP over this six year period comprised four sequential phases, corresponding to four different arrangements for housing the fiducials:

Phase 1	June 1994 - May 1995	adhesive fiducials attached directly to the scalp
Phase 2	June 1995 - June 1996	fiducials in prototype halo, skull-mounted with a screw in the outer table or scalp-mounted with tape
Phase 3	July 1996 — June 1998	prototype halo, scalp-mounted with sutures
Phase 4	July 1998 — June 2000	production halo, scalp-mounted with sutures

Demographic details were recorded as well as the clinical presentation and course, imaging findings (characteristics of the intracranial lesions, number, location and size), surgical operation (hospital, anaesthesia, details of the surgery performed), postoperative course, complications and outcome. Hospital folders (including microfilmed records where necessary), Radiotherapy departmental folders, and Radiology departmental records were reviewed for each patient. This data was entered on an Excel spreadsheet, a summarized version of which may be found in Appendix I.

A data sheet was used to log details at the time of the stereotactic CT scan; this scan was available at the time of writing for all but two patients.

5.2 Procedure

The indications for surgery in 100 patients included biopsy or aspiration of a lesion, implantation of a catheter to decompress a tumour cyst or divert CSF and craniotomy to resect a tumour (Figure 5.1).

An intracranial mass was biopsied in 65 patients while 14 patients underwent cannulation of a craniopharyngioma for implantation of an Ommaya reservoir. Fifteen patients underwent aspiration of a collection, most commonly an abscess (12); and a small number underwent stereotactically guided insertion of a shunt (3) or resection of a tumour (3).

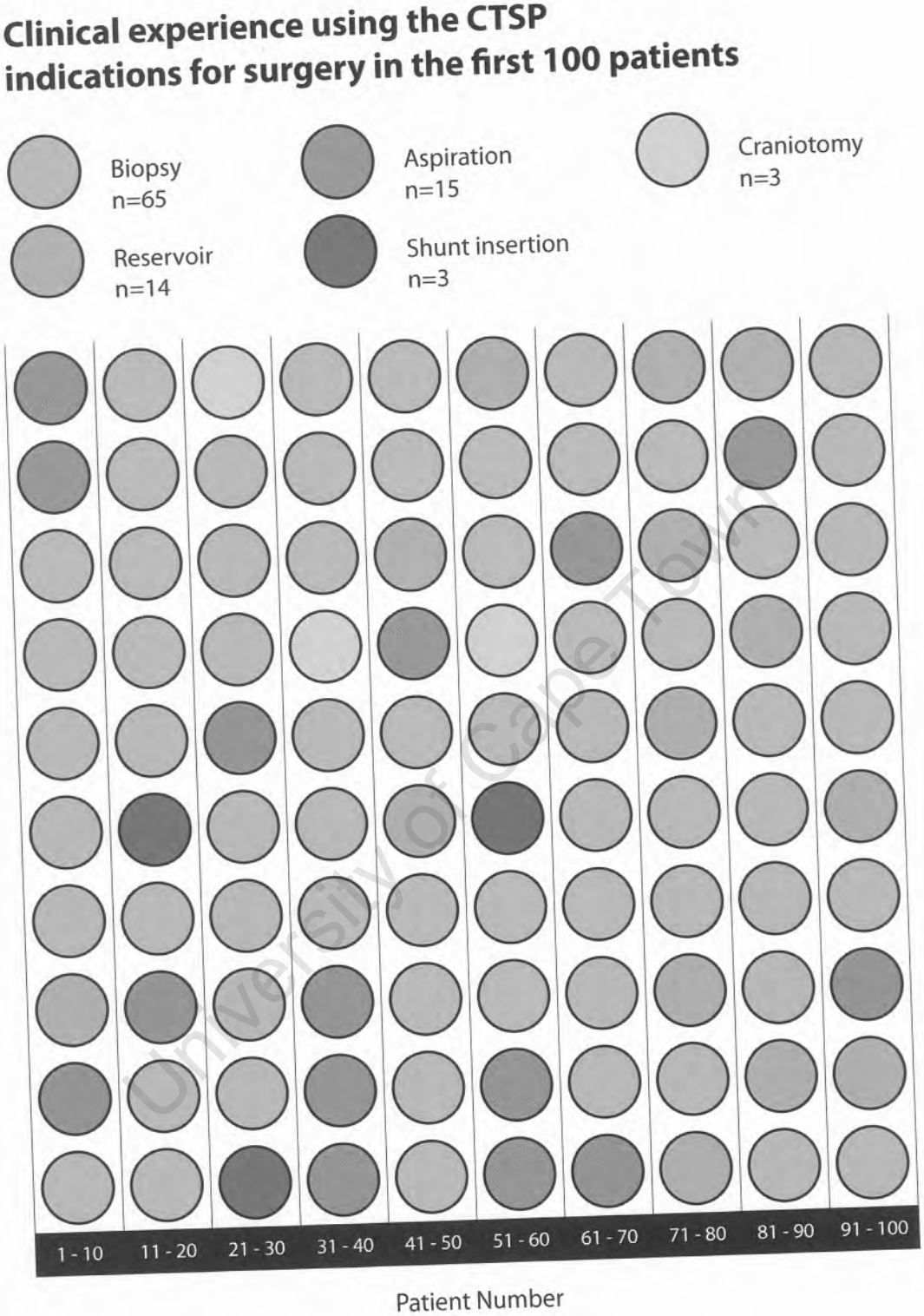


Figure 5.1: Procedure performed in the cohort of 100 patients

5.3 Diagnosis

A neoplasm was present in 75 patients, most commonly an astrocytoma (36), while 15 patients harboured a cerebral metastasis and 14 had a craniopharyngioma. CNS infections, most commonly cerebral abscesses, accounted for 18 cases and hydrocephalus was treated in 3 patients. Two of the remaining 4 patients had infarcts, one had a giant capillary cavernous angioma and one had basal ganglia calcification due to tuberose sclerosis.

Due largely to challenges in making a histopathological diagnosis, particularly early in the series, there was a difference between the initial diagnosis and the patient's final diagnosis, and this is shown in Table 5.1.

Diagnosis			**Diagnosis at procedure**		**Final diagnosis**
Astrocytoma			**31**		**36**
	GBM	11		14	
	Grade III	15		16	
	Low grade	5		6	
Metastasis			**16**		**15**
Craniopharyngioma			**14**		**14**
Other primary tumour			**7**		**10**
Infection			**15**		**18**
CSF abnormalities			**3**		**3**
Other			1		**4**
Non-diagnostic: system or surgeon error			**5**		**N/A**
Non-diagnostic: inconclusive histology			**8**		**N/A**
Total			**100**		**100**

Table 5.1: Initial diagnosis and final diagnosis in 100 patients. Astrocytomas were graded according to the WHO classification [Kleihues]

5.4 Repeat surgery

These 100 patients underwent 115 operations, of which 72 were biopsies (62.6%), while 18 lesions such as abscesses and parasitic cysts were aspirated (15.7%). Intracranial catheters were introduced under stereotactic guidance in the remaining 21.7% of cases; either to implant an Ommaya reservoir in a cystic craniopharyngiomas in 18 instances (15.7%), divert CSF in 4 cases (3.5%) or guide stereotactic craniotomies in 3 cases (2.6%).

Thirteen patients underwent more than one stereotactic procedure, with 11 patients having two operations and 2 having three operations.

Seven patients each underwent two successful operations; three patients with brain abscesses required a second procedure to tap a new collection (Cases 61, 89 and 93), two patients underwent a second stereotactic insertion of an Ommaya reservoir (Cases 3 and 71) and repeat surgery for CSF diversion was required in one child (Case 55). Two biopsies were repeated, in one case for a new lesion (Case 40) and in the other, for new symptoms (Case 42).

Two patients underwent successful implantation of an Ommaya reservoir following an initial unsuccessful operation; the first patient required revision of a catheter which had been misplaced at the first operation (Case 48), while the second experienced a significant haemorrhage necessitating termination of the first procedure (case 80).

One patient underwent two biopsies that were both non-diagnostic (Case 75), while two patients each underwent a third biopsy following two biopsies that failed due to incorrect use of the system. The third biopsy was diagnostic in one patient (Case 77), while in the other it was partially successful in that histology was abnormal but inconclusive (Case 79). These cases are reviewed in detail elsewhere.

No	Dates	Reason for repeat surgery	
3	19940707 19950119	New loculated craniopharyngioma cyst developed, separate from previous Ommaya reservoir	Both successful
40	19961205 19970825	Biopsy of new lesion	Both successful
42	19970116 19971106	Re-biopsy of lesion for new symptoms	Both successful
48	19970422 19970429	Misplacement of catheter when cannulating craniopharyngioma	2^d procedure successful
55	19970728 19970814	Revision of ventricular catheter	Both successful
61	19970912 19970916	Re-accumulation of abscess	Both successful
71	19980206 19980226	Re-siting of catheter in craniopharyngioma to avoid traversing ventricle	Both successful
75	19980317 19980324	No diagnosis	Both failed
77	19980720 19980728 19980817	No diagnosis No diagnosis	3rd biopsy successful
79	19980921 19980929 19981012	No diagnosis No diagnosis	3rd biopsy partially successful
80	19981006 19981103	First operation to implant Ommaya reservoir in craniopharyngioma terminated because of haemorrhage	2nd procedure successful
89	19990518 19990603	Re-accumulation of abscess	Both successful
93	19990806 19990811	Re-accumulation of abscess	Both successful

Table 5.2: Repeat procedures

5.5 Demographics of the patient cohort

This study spans a period of six years, from June 1994 to June 2000 (Figure 5.2).

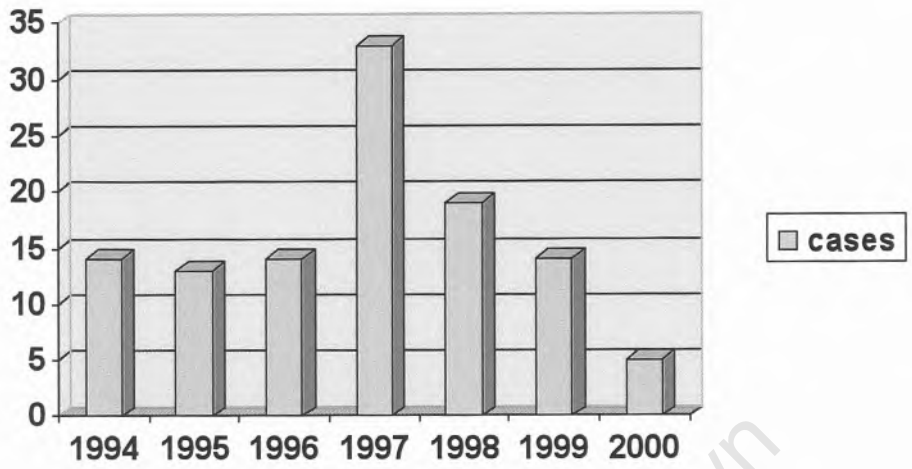


Figure 5.2: Distribution of patients from 1994 to 2000 (n=100).

The 100 patients comprised 53 males and 47 females.

Twenty two of the patients were children aged 16 or younger, who underwent a total of 27 stereotactic procedures (23.5% of the total).

Five of the patients were adults aged 70 or older.

The median age of the cohort was 36 years, as was the mean age.

5.6 Clinical presentation

Details of each patient's presenting symptoms and signs were documented.

As all the patients had an intracranial space-occupying lesion, it is not surprising that headache (53%) and focal deficits (50%) were most commonly noted.

Altered higher mental function (drowsiness or personality change) prompted investigation in 31% while 30% had seizures.

Visual symptoms, most commonly reduced acuity and diplopia, occurred in 19%, while 14% had a variety of other symptoms, ranging from macrocrania to endocrine dysfunction.

*Presenting symptom**	Astrocytoma *I/11* (n=6)	Astrocytoma III/IV (n=30)	Metastasis (n=15)	Craniopharyngioma (n=14)	Other tumour (n=10)	Infections (n=19)	Other (n=6)
Altered mental status		14	4	4	5	5	
Headache	1	17	8	11	4	10	2
Seizures	3	11	5		4	8	
Focal deficit	4	13	11	2	7	12	1
Visual symptoms	1	3	3	10	2		
Other		1		6	3		4

Table 5.3: Presenting symptoms of patients sorted by diagnosis.

* a patient may have presented with more than one symptom.

5.7 Imaging findings

5.7.1 Enhancement characteristics

A varying degree of enhancement of the lesion on CT scan following administration of IV contrast was seen in 90 cases. Of these, 13 enhanced uniformly and avidly, 35 enhanced inhomogenously and 28 showed peripheral "ring enhancement". Fourteen cystic suprasellar tumours showed enhancement as well as calcification in either the associated solid component or the capsule. Five low density lesions did not enhance at all and five lesions were CSF density collections.

5.7.2 Location

The targeted lesion was located in the right hemisphere in 51 cases (44.3%), the left hemisphere in 31 cases (27%) and the midline in 33 cases (28.7%).

The majority of lesions were deep (45.5%), with 19 suprasellar lesions, 13 lesions located in the genu, rostrum, body or splenium of the corpus callosum, 2 lesions in the midbrain and 1 in the quadrigeminal cistern. The lateral ventricle was the target in 5 cases (4.3%), 24 lesions were in the deep white matter (20.1%) and 34 in the subcortical white matter or cortex (29.6%).

Location	Right	Midline	Left
Midbrain	2		
Quadrigeminal cistern		1	
Suprasellar		19	
Corpus callosum		13	
Basal ganglia and thalamus	12		5
Lateral ventricle	3		2
Deep white matter	17		7
Subcortical white matter	10		6
Superficial Cortex	7		11
Total	51	33	31

Table 5.4: Anatomical location of lesions

5.7.3 Volume

As stereotaxis was generally only used when a freehand approach was considered likely to fail, or had failed, the lesions were generally small.

Volume was estimated as for a spherical structure by multiplying the largest cross-sectional diameters in three planes, multiplied by ri/6 ({X*Y*Z}*{22/42}) [Bernays].
Lesions ranged in volume from 0.52 ml to 70.7 ml, with a mean volume of 14.5 ml and median volume of 9.4 ml (interquartile volume 4.2 ml — 18.8m1).

The distribution of lesion volumes is shown in Figure 5.3; the values on the abscissa reflect lesion volumes based on an average diameter of 10mm (5_0.53m1); 10-20 mm (s4.2m1); 20-30 mm (<14.2m1); 30-40 mm (5_33.5m1) and >40mm (33.5m1).

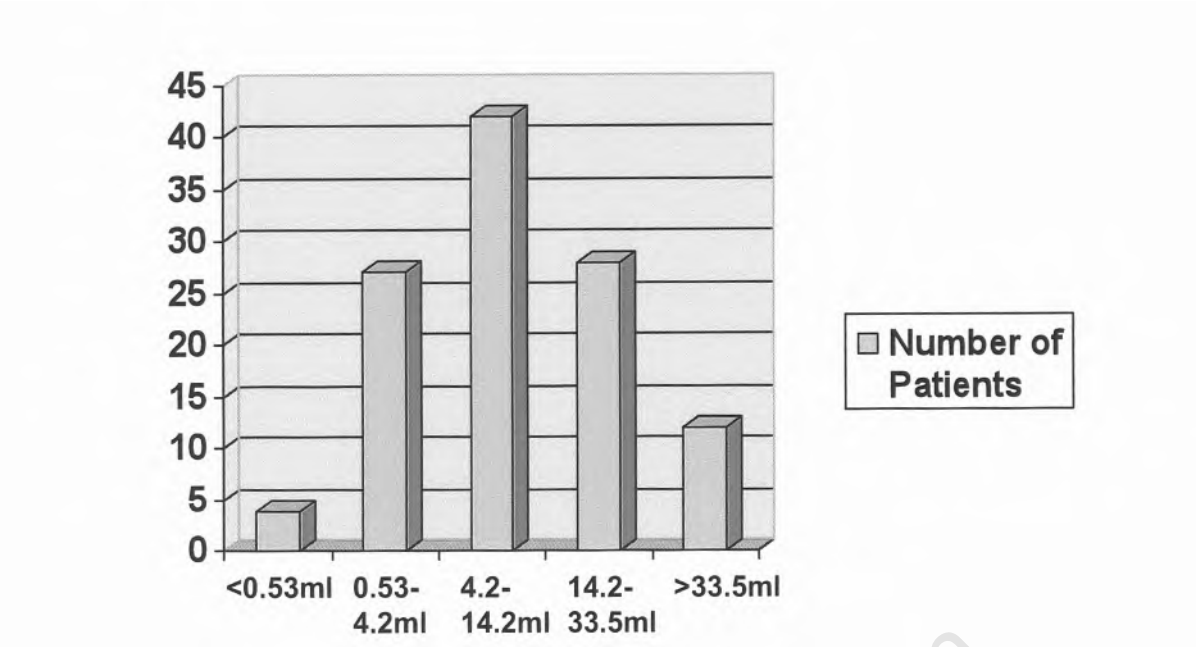


Figure 5.3: Distribution of lesion volumes (n=113)

5.8 Management

The majority of operations took place at Groote Schuur Hospital (88.7%), while 13 (11.3%) took place at Red Cross Children's Hospital.

5.8.1 Surgeons

In all, 19 surgeons were involved in these cases with a cumulative number of 200 surgeons/ 115 cases. At least one of the two neurosurgeons (AGF and AGT) involved in developing this system performed each of the first 32 cases and these two surgeons participated in 44 and 43 operations respectively. Two fellow registrars (HAE and GAW) subsequently became involved, participating in 24 and 21 cases, of which they were lead surgeon in 11 and 12 cases respectively.

The first 50 patients in this series underwent a total of 54 operations, of which 49 (90.7%) were done by AGF and/or AGT, while the second 50 patients underwent 61 operations, of which only 21 (34.4%) were done by AGF or AGT.

Six other colleagues served as lead surgeon in a total of 22 cases (median n=4); all told, 45 cases (39%) were done by surgeons other than AGF and AGT. Although this was desirable as the purpose was to develop a system that would be widely used, this may also have been a factor in the delayed recognition of a problem during the transition from the prototype to the production version of the CTSP as will be discussed later.

5.9.2 Minor complications

Eighteen patients experienced minor complications, none of which was permanent.

Superficial wound infection occurred in one patient following aspiration of an abscess (Case 33). This patient had negative HIV serology, but had a past history of pulmonary tuberculosis and had therefore been commenced on antituberculous drugs, steroids and intravenous antibiotics two weeks prior to surgery for a ring-enhancing lesion which had gradually enlarged. Three days after his stereotactic procedure he had evident wound sepsis; however, this was superficial and required nothing further than local dressings. A second operation was required to re-tap the abscess.

Transient neurological complications occurred in eight patients. Mild postoperative worsening a pre-existing motor deficit was noted in three patients (Cases 10, 27 and 59) but this did not persist. One patient was noted to have new onset of dysphasia (Case 94), curiously enough after biopsy of a lesion in the right frontal lobe, and this also resolved. Delayed waking from anaesthesia or transient reduction in their level of consciousness was noted in four patients, following biopsy (Cases 16 and 34), craniotomy (Case 57) and cannulation of a large cystic craniopharyngioma (Case 73).

Four patients experienced transient neuro-endocrine complications following insertion of an Ommaya reservoir into a craniopharyngioma cyst ; three developed diabetes insipidus (Cases 48, 92 and 95), while one experienced hypothalamic dysfunction with an episode of bradycardia intra-operatively upon puncturing the craniopharyngioma cyst followed by transient postoperative hypothermia (Case 3).

Adverse effects of drugs occurred in eight patients with seven developing rashes due to anticonvulsants (Cases 19, 32, 37, 57, 69, 91 and 94) and steroid-induced hyperglycaemia in one (Case 16). Only four of the seven patients who developed an anticonvulsant-induced skin rash had presented with seizures. One patient had a documented deep venous thrombosis (Case 19).

No	Date	Complication	Outcome
3	19940707	bradycardia when inserting catheter in craniopharyngioma and **transient postoperative hypothermia**	No sequelae
10	19941027	**Transient weakness left leg**	Resolved
16	19950131	**Transient drowsiness** and steroid-induced hyperglycaemia	Resolved
19	19950302	Anticonvulsant rash and DVT	No sequelae
27	19960305	**Transient weakness left leg**	Resolved
32	19960516	Anticonvulsant rash	No sequelae
33	19960523	**Wound sepsis** (following abscess tapping)	No sequelae
34	19960606	**Delayed waking from anaesthesia**	Resolved
37	19960822	Anticonvulsant rash	No sequelae
48	19970429	**Transient exacerbation of diabetes insipidus**	Resolved
57	19970818	**Transient confusion &** anticonvulsant rash	Resolved
59	19970902	**Transient weakness right leg**	Resolved
69	19971212	Anticonvulsant rash	No sequelae
73	19980305	**Delayed waking from anaesthesia**	No sequelae
91	19990622	Anticonvulsant rash	No sequelae
92	19990707	**Transient diabetes insipidus**	Resolved
94	19991018	**Mild dysphasia,** anticonvulsant rash	Resolved
95	19991116	**Transient diabetes insipidus**	Resolved

Table 5.7: Minor complications

5.9.3 Postoperative CT scan

The majority of patients (104/115; 90.4%) underwent a postoperative CT scan. This was done in all cases where a catheter was implanted in order to check the position and in most cases where an abscess was aspirated; although aspiration of pus at the time of surgery convincingly confirmed the operative objective had been met, 66% of these patients required further CT scans to monitor their response to antibiotics.

Sixty out of the 71 (84.5%) patients who underwent a stereotactic biopsy had a postoperative CT scan, most within the first 24 hours (68.3%). The primary purpose of this was to establish that there was no intracranial haematoma, but often this scan also revealed the site where the biopsy was taken, as indicated by a small fleck of haemorrhage. Thirteen patients (21.6%) were scanned more than three days after biopsy, by which time an assessment of intracranial blood was considered less helpful.

Twenty patients (42.6%) had no blood evident on the postoperative CT scan; of the 27 (56.4%) in whom a haematoma was seen, this was greater than 1cm in diameter in only four (14.8%). All but one of these haematomas were intracerebral, the only exception being a small surface haemorrhage in a patient who underwent biopsy of a cortical lesion (Case 27).

The patient who experienced a substantial intraoperative haemorrhage upon attempted puncture of a craniopharyngioma underwent scan following craniotomy and this confirmed an extensive subarachnoid haemorrhage (Case 80). No patient underwent further surgery to evacuate a clinically silent haematoma disclosed by a routine CT scan. The problem was clinically apparent in both patients who underwent craniotomy, either manifesting with sudden postoperative deterioration in GCS (Case 75) or torrential intraoperative bleeding (Case 80).

	No	Y: <5mm	Y: 5-10 mm	Y: 10-30 mm	Y: 30-40 mm	Total
Day 0	1	2	1	0	1	5
Day 1	16	6	11	3	1	36
Day 2	1	**0**	1	0	0	2
Day 3	2	1	1	0	0	4
Total	**20 (42.6%)**	**9 (19.1%)**	**14 (29.8%)**	**3 (6.3%)**	**2 (4.2%)**	**47**

Table: 5.8: Presence of haemorrhage on the postoperative CT scan

5.10 Outcome of stereotactic biopsy

Histology was obtained in 74 cases, as the three craniotomies were preceded by an initial biopsy. Of the 71 isolated biopsies, the Backlund spiral biopsy needle was used in the first 14 cases, 2 of which had an additional specimen taken with the Melvill aspiration needle, while the Sedan side-cutting biopsy needle was used for the remaining 57 cases.

An incidental finding was a difference in diagnostic rates with the two biopsy needles used in this study. Of the eight biopsies that yielded tissue that was inconclusive, 7 occurred in the first 14 biopsies, a rate of 50%. These biopsies were all taken with the spiral biopsy needle, and the pathology report usually made reference to the small size of the specimen.

This biopsy needle was replaced with a side-cutting Sedan needle from Case No 22 onwards. A total of 60 biopsies were performed with the Sedan needle and if one excludes the cases that where the biopsy was compromised by system or surgeon error, only one (1/51) biopsies was

inconclusive. Fisher's exact testing revealed this finding to be significant (p<0.001), however this result needs to be interpreted with caution due to the developmental nature of this project. Furthermore, patients were not biopsied with both needles, hence this retrospective comparison may be flawed.

No	Date	Problem	Solution
1	19940606	Abnormal tissue (calcified neuropil) but **non-diagnostic**	Biopsy needle
6	19941006	?High grade glioma; GBM at craniotomy	Biopsy needle
8	19941020	Abnormal tissue (non-specific necrosis) but **non-diagnostic**	Liaison with Pathologist
12	19941117	Smear ?GBM; histo uncertain histogenesis	Biopsy needle
14	19941201	Abnormal tissue obtained (vessels and haemosiderin-laden macrophages) but **non-diagnostic.** Subsequent craniotomy also non-diagnostic	Biopsy needle
17	19950214	?Low grade glioma	Biopsy needle
20	19950316	AIDS; Nonspecific inflammatory	Biopsy needle
79	19981012	*Non-diagnostic*	Calibration data corrected; likely inflammatory process such as TB

Table 5.9: Inconclusive histology

An intraoperative smear preparation was performed in 60/71 biopsies (81%). The final histological diagnosis concurred with the smear diagnosis in 43 cases (71.7%) (Table 5.9).

Metastatic lesions were correctly diagnosed on smear in 13 cases (100%), while of the 22 astrocytomas, 19 were correctly identified as glial on smear (86.3%). Astrocytomas were graded using the WHO classification [Kleihnes] and this proved to be challenging on smear, with an incorrect grade assigned in 6/19 (31.6%).

	Astrocy-toma Grade I - II	Astrocy-toma Grade III	Astrocy-toma Grade IV	Metasta-sis	Other tumour	2Non-neoplas-tic	Total
Smear correct	2	7	4	13	4	7	**37**
Smear correct, wrong grade	0	4	2	N/A	N/A	N/A	**6**
Smear wrong	**0**	1	2	0	2	2	**7**
No smear	4	4	5	0	1	32	**16**
	0	1	0	0	2	2	**5**
Total	6	17	13	13	9	13	**71**

Table 5.10: Accuracy of the smear stratified for different pathologies.

'Invalid: the smear was considered invalid for this pathology if there was a sampling error

[2] Non-neoplastic: includes infective/ inflammatory conditions and vascular lesions

[3] Frozen section rather than smear was done on two cases at Red Cross Hospital

5.11 Outcome of stereotactic cannulation

Fourteen patients underwent a total of 18 stereotactic operations, with four patients requiring repeat surgery for different reasons in each case. One patient experienced progression of a separate cyst and required a second reservoir to treat this (Case 3), and in another patient, a second catheter was inserted in a new trajectory under stereotactic guidance as the initial catheter traversed the lateral ventricle and a leak was noted on the contrast cystogram (Case 71).

The cyst wall was not penetrated on two occasions. In one instance, clear fluid resembling CSF was aspirated at the time of surgery and the postoperative CT scan confirmed that the distal tip of the catheter was in the subarachnoid space alongside the tumour cyst (Case 48), while in the second case significant haemorrhage was experienced while attempting to penetrate cyst wall, resulting in the abandonment of the stereotactic procedure (Case 80). Both patients underwent successful stereotactic implantation at their second procedure.

In one case the lesion was missed altogether due to a system calibration error which was only recognized postoperatively (Case 78) and this patient subsequently underwent microsurgical excision.

The cyst was cannulated at the first operation in eleven of the remaining thirteen patients (84.6 %), but the procedure was considered *entirely successful* in only 7/11 (60%) as four experienced catheter-related complications. In two cases the postoperative CT scan showed the tip to be abutting the distal wall of the cyst; a minor revision was performed in one patient (Case 95) where the catheter was pulled back one centimeter in order to reduce the risk of perforation and subsequent leakage of bleomycin, but this was not done in the other patient (Case 90) as bleomycin was not administered. In two further cases, the cyst was initially aspirated, yielding fluid typical of a craniopharyngioma but the surgeon did not implant a reservoir as there was uncertainty as to whether the tip had remained located in the cyst (Figure 5.4.).

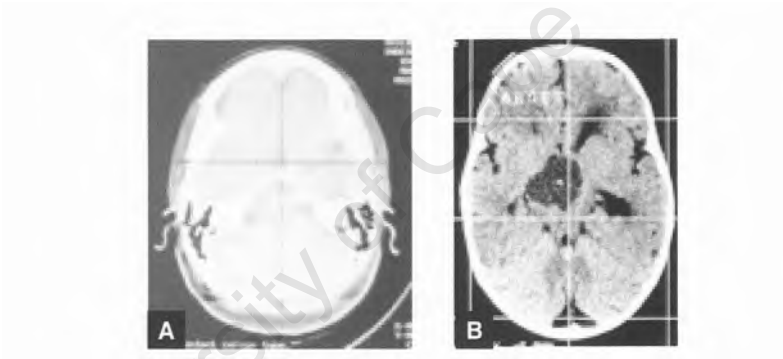


Figure 5.4: Failed implantation of Ommaya reservoir following successful cyst cannulation. Stereotactic planning scans of two patients in whom the catheter tip was not adequately secured in the tumour cyst. The catheter was withdrawn in the patient on the left (Case 60), whose cyst in hindsight was clearly too small for this treatment strategy. The catheter was left in situ in the patient on the right (Case 92) and he subsequently underwent craniotomy and subtotal resection.

In the first such instance, the cyst was particularly small with a volume of 0.8 ml (Case 60). The patient was scheduled for craniotomy but the cyst was no longer visible on the preoperative CT scan and she subsequently remained clinically stable for 5 years before progressing and requiring surgery.

In the second instance, the cyst was initially entered but the flow of cyst fluid ceased upon withdrawal of the Seldinger guide-wire and re-insertion of the catheter failed to produce a convincing restoration of flow of tumour fluid; the preoperative cyst volume in this case was 25.7m1 (Case 92). The postoperative CT scan confirmed decompression of the cyst but the patient went on to have a craniotomy in view of the residual solid component.

All the cases are summarized in Table 5.11.

No	Age	Date	Comments
3	9	19940707 19950119	Tumour diagnosed 3 years previously at a peripheral hospital where a VP shunt was inserted; she was referred for management of her progressive diencephalic syndrome. The first stereotactic operation uncomplicated but a second catheter was required 6 months later for a new loculated cyst, not in communication with the existing Ommaya reservoir.
45	15	19970318	Initial craniotomy at age 5; cystic recurrence. Uncomplicated procedure.
48	5	19970422 19970429	First catheter misplaced hence second operation required. The Modified Seldinger technique used to penetrate cyst at 2nd operation.
60	16	19970905	Craniotomy and resection at age 14; presented 2 years later with headache and a small cyst. The stereotactic procedure was successful in that the cyst was aspirated, but was too small to retain the distal end of the catheter.
71	49	19980206 19980226	Catheter inserted successfully, but revised as noted to be traversing ventricle on postoperative CT scan.
73	25	19980305	Uncomplicated procedure.
76	6	19980622	Uncomplicated procedure.
78	6	19980915	Lesion missed (calibration error)
80	13	19981006 19981103	Haemorrhage on first attempt; second operation uneventful.
82	53	19981201	Uncomplicated procedure.
87	14	19990216	Craniotomy and resection at age 10; cystic recurrence. Uncomplicated procedure.
90	1.5	19990527	Uncomplicated procedure; distal end of catheter in too far on follow-up scan but not revised as marked clinical improvement with simple decompression and decision made not to instill bleomycin.
92	6	19990707	Stereotactic procedure successful in that the cyst was aspirated, but unable to maintain position of distal end within the cyst when decompressed.
95	8	19991116	Cystic recurrence while undergoing proton therapy 4 months after craniotomy and subtotal removal; successful insertion but tip in too far on follow-up scan therefore revised (pulled back 1 cm).

Table 5.11: Patients undergoing stereotactic cannulation with intent to implant an Ommaya reservoir

5.12 Overall outcome

All three stereotactic craniotomies were successfully completed, as were all four of the CSF diversion procedures.

Apart from one abscess that could not be aspirated stereotactically due to brain shift, all procedures where the goal was to aspirate an abscess or cyst were successfully concluded (18/19; 94.7%).

As discussed above, eighteen craniopharyngiomas were to be cannulated and this was achieved in thirteen (72.2%). Two cases were partially successful in that the cyst was entered, but could not be completed as the cyst was decompressed to the extent that the tip of the cannula could not be secured within the cyst (2/18; 11.2%). Three cases failed (3/18: 16.6%), two because of an error in technique on the part of the surgeon (Cases 48_1 and 80_1) and one because of incorrect use of the system (Case 79).

Of the 71 stereotactic biopsies performed, 54 were unequivocally successful in yielding diagnostically accurate pathological tissue (76.1%).

As discussed in Chapter 5.10, abnormal tissue was obtained at biopsy in a further eight cases (11.3%), but there was some doubt as to the exact diagnosis (Table 5.9); these were considered to be partially successful and in only two cases (Cases 6 and 79_3) did this have a significant clinical impact.

Biopsy failed in eight patients (12.6%); failure was considered to be due to a system error, directly attributable to development of the system in two cases, with both leading to a fundamental change to the system (Cases 5 and 28). Three operations in two patients (4.2%) reflected surgeon error, in attempting to biopsy an intraventricular tumour (Case 67) and failure to biopsy a tumour which was later found at craniotomy to be a meningioma (Case 75_1 and 75_2). Four biopsies failed immediately after the transition from the prototype to the production system, due to incorrect use of the system (Cases 77 1 and 77_2; Case 79_1 and 79_2).

In total, 13 procedures failed. Two failures revealed deficits in the system that were subsequently corrected (the configuration of the fiducials and the method of securing the halo) and six reflected errors in surgical judgment, which perhaps reflects a "learning curve" of decision-making. Failure occurred in five out of six cases performed immediately after the introduction of the production

system as a consequence of failing to amend the calibration data in the software program. These six operations were performed by four different lead neurosurgeons, which may have contributed to the delay in recognizing that there was a problem.

No	Date	Problem	Error	Solution
2	19940630	Brain shift, stereotactic procedure **abandoned**	**0**	Anaesthetist awareness
5	19940906	Fiducials transposed. stereotactic procedure **abandoned**	**a**	New configuration (J6)
28	19960326	Lesion missed- **normal** brain tissue obtained	**a**	More secure technique for attaching halo
48	19970325	Unable to penetrate craniopharyngioma cyst	**0**	Modified Seldinger technique
67	19971209	Lesion missed- **normal** brain tissue and choroid plexus obtained	**0**	Avoid stereotactic biopsy of intraventricular lesions
75	19980317	**Non-diagnostic** - likely lesion not penetrated	**0**	Biopsy technique
	19980324	**Non-diagnostic** - likely lesion not penetrated	**0**	Biopsy technique
771	19980720	**Non-diagnostic**	13	Calibration data
77_2	19980728	**Non-diagnostic**	13	Calibration data
78	19980915	Lesion missed- stereotactic procedure **abandoned**	13	Calibration data
79_1	19980921	**Non-diagnostic**	13	Calibration data
79_2	19980929	**Non-diagnostic**	13	Calibration data
80_1	19981006	**Intraoperative haemorrhage**	**0**	Modified Seldinger technique

Table 5.12: Failed procedures

Error classification:

a: error due to failure of the stereotactic system

[3: error due to incorrect use of the system

0: error due to surgical technique

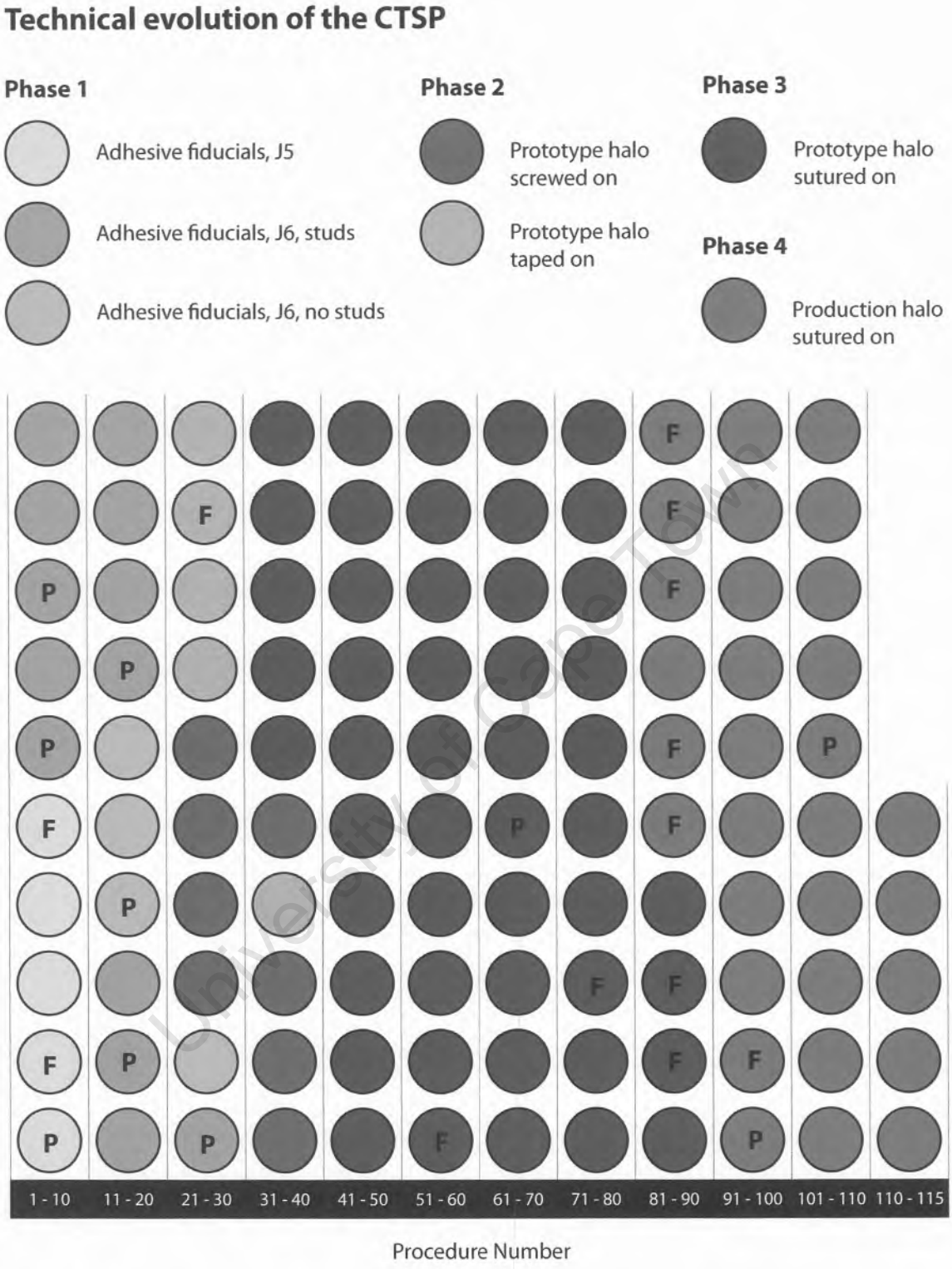


Figure 5.5: Failures due to system or surgeon errors and non-diagnostic biopsies due to inconclusive histology during the 115 operations.

F: Failures

P: Partial failures (inconclusive histology or Ommaya not implanted)

Each of the cases that failed due to system or surgeon error will be reviewed in detail in order to highlight the lessons learnt. Cases with inconclusive histology will be reviewed in Chapter 6.10.

The data are summarized in Table 5.9, stratified for success and failure in terms of the four phases defined previously.

	Phase 1	**Phase 2**	**Phase 3**	**Phase 4**	**Total**
Period	June 1994 — May 1995	June 1995 — June 1996	July 1996 – June 1998	July 1998 – June 2000	
Fiducials	Applied directly to scalp with adhesive doughnut	Halo screwed into outer table or stuck on with tape	Prototype halo sutured onto scalp	Production halo sutured onto scalp	
Number of patients	21	13	42	24	100
Objective fully met	13	12	44	23	92
'Partial success	7	0	1	2	10
Failures due to surgeon errors	1	0	4	1	6
Failures due to system errors	1	1	0	5	7
Number of procedures	**22**	**13**	**49**	**31**	**115**

Table 5.13: Results of 115 stereotactic procedures, stratified according to the 4 phases in the development of the CTSP.

'Partial success was either inconclusive histology (8 cases) or aspirating a cystic craniopharyngioma but failing to secure a catheter in the cyst (2 cases).

Overall, the procedural objective was unequivocally met in 92/115 cases (80%), but this needs to be analysed in context. The project described in this thesis started off with a prototype which underwent 5 major iterations (adhesive doughnut fiducials > tacks > halo screwed on > halo taped on > halo sutured on) before the production version was introduced, at which time a further "developmental" problem occurred, in that incorrect calibration data was used for six cases (although one of the patients fortuitously had a diagnostic biopsy).

Furthermore, targeting was accurate in the ten cases classified as "partial success" in that the inconclusive biopsies revealed pathological tissue in all eight cases and both craniopharyngiomas were initially entered upon passage of the cannula.

If one *excludes* the six cases over the period when the incorrect calibration data was used and one *includes* as successes the ten cases in which targeting was correct, the surgical objective was realized in 101/109 cases (92.7%).

Case Illustrations

The ten patients who underwent a total of thirteen failed procedures will now be reviewed in detail.

Case 2

A 46 year old female awaiting cardiac transplant for Eisenmenger Syndrome developed sudden right-sided retro-orbital pain and headache. Head CT scan showed 2 small ring-enhancing lesions in the right frontal lobe and right parietal lobe.

Stereotactic aspiration was attempted via a right frontal burr-hole under general anaesthesia; when the dura was incised, a one centimeter space was found between the dura and the brain, most likely due to over-enthusiastic anaesthetic management of suspected raised intracranial pressure. This brain shift had altered the position of the lesion, which was clearly deeper and was aspirated freehand after determining the correct trajectory with the aid of the stereotactic device.

Course:Negative culture; patient commenced on intravenous antibiotics and remained under the care of Cardiology.

Final diagnosis:Brain abscess

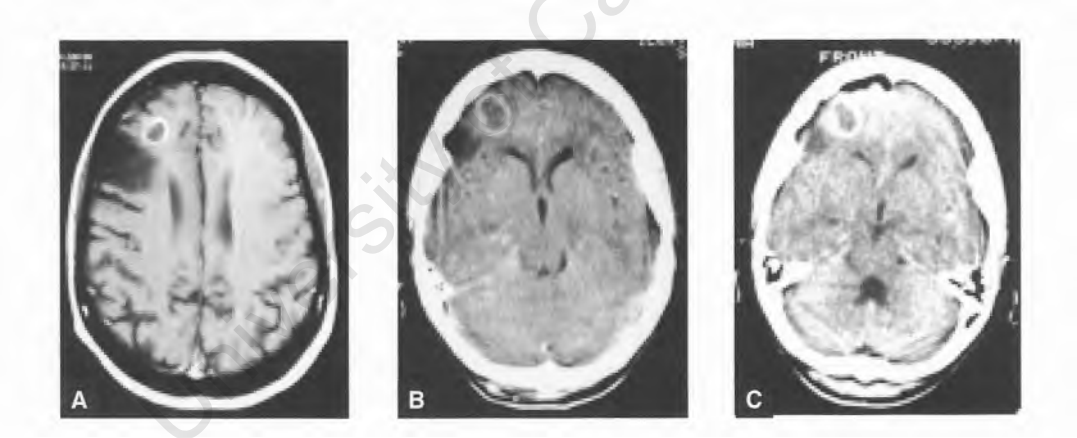


Figure 5.6: Axial T1 MRI scan (a) and CT scan, both with IV contrast, show a right frontal subcortical ring-enhancing lesion adjacent to an infarct. Following aspiration, the lesion was smaller on the postoperative scan (c), which also demonstrated an adjacent locule of subdural air.

Problem:Management error. Brain shift due to iatrogenic brain shrinkage

Solution:Care taken to ensure that the Anaesthetist understands the importance of maintaining intracranial homeostasis.

Case 5

A 25 year old female presented with a 3 week history of headache, neck stiffness and left hemiparesis; she was on treatment for cervical carcinoma-in-situ and known to be HIV+ with human papilloma virus infection and condylomata accuminata. Serology for toxoplasmosis, cryptococcus and syphilis was negative. The fiducials were attached to her scalp in the ward, following which a CT scan was done to localize the target. The patient was taken to the Operating Theatre while the data was entered and the setting diagram printed; when the trajectory was checked prior to starting the case it was clearly incorrect. An attempt was made to biopsy the lesion freehand after placing the burr-hole at the pre-determined entry point, but this was non-diagnostic.

Course: The patient was commenced on 4-drug TB therapy as well as pyramethamine/ sulphadiazine, dexamethazone and phenytoin; despite this, she continued to deteriorate and treatment was stopped after one month.

Final diagnosis: Unknown, most likely Primary CNS Lymphoma

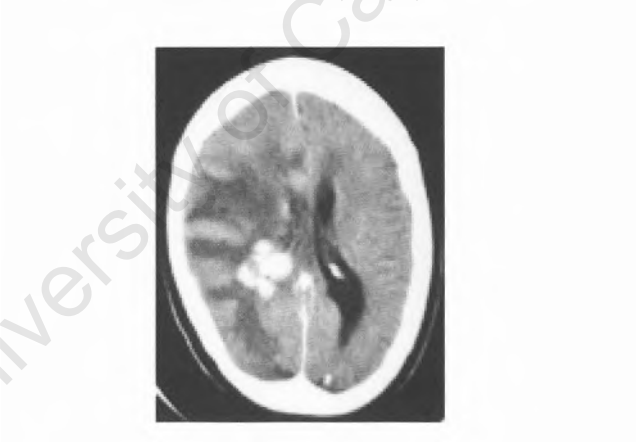


Figure 5.7: Lobulated lesion in the trigone of the right lateral ventricle with extensive low density throughout the white matter of the hemisphere, enhancing brightly following administration of intravenous contrast.

Problem: Technical error. Two of the fiducials were transposed when entering data from the CT scan into the program and the software was unable to detect the error as the fiducials were in an equilateral triangle configuration, hence two solutions were possible.

Solution: Configuration of fiducials changed from equilateral triangle to an isosceles triangle to ensure there was only one possible position for the pointer to be mounted. This necessitated the manufacture of a new pointer, the 'A".

Case 28

A 43 year old female presented with a 3 month history of stiffness and numbness of the left foot; she was systemically well with no past medical history of note. CT scan showed seven ring-enhancing lesions widely distributed though the brain; all other investigations were negative.

Stereotactic biopsy of right parietal lesion after attaching halo with tape showed normal brain.

Course:Four drug TB therapy was commenced for a presumptive diagnosis of multiple tuberculomas and follow-up imaging two months later showed the lesions had resolved; the patient remained well at long-term follow-up.

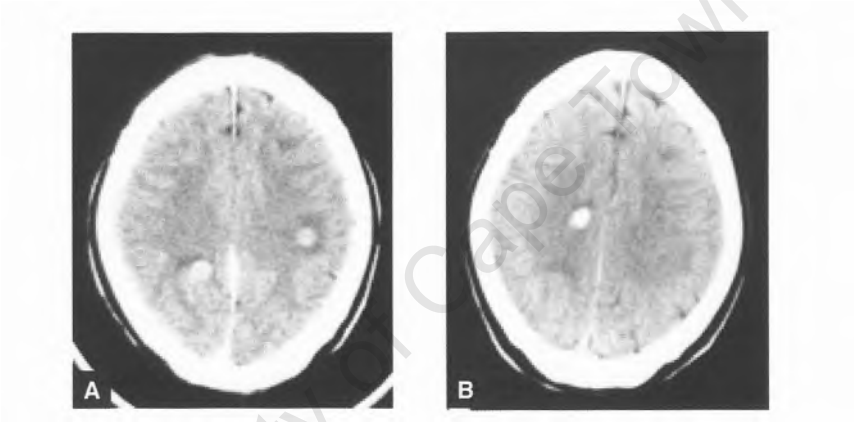


Figure 5.8: Axial CT scan showing ring-enhancing lesions with surrounding low density (a). Follow-up CT one day after biopsy shows a small haematoma in the deep white matter, some distance away from the planned target.

Problem: Technical error. Technique for securing halo using adhesive tape not reliable enough.

Solution:A more secure technique was required for attaching the halo.

Case 48

This 5 year old boy from a rural area developed headache and visual loss following a minor head injury and was referred to the Red Cross Children's Hospital Trauma Unit with a deteriorating level of consciousness 5 days later. CT scan showed acute hydrocephalus and a suprasellar cyst with a mineralized wall, highly suggestive of craniopharyngioma. The patient underwent urgent VP shunt insertion bilaterally and postoperatively his level of consciousness improved promptly but he had ongoing features of pituitary dysfunction and poor vision, particularly on the left.

A decision was made that he would best be managed by instillation of bleomycin into the cyst and one week later implantation of an Ommaya reservoir was attempted using stereotactic guidance. Upon inserting a catheter with the stylet in place, correct placement was suggested by the fact that firm resistance was felt when the cyst was encountered, but when the catheter was passed to the predetermined depth, clear fluid resembling CSF was aspirated. Follow-up CT scan showed the catheter tip to be located in the subarachnoid space adjacent to the tumour, seemingly deflected by the dome of the cyst.

One week later, the patient was taken back to the Operating Theatre where the halo was applied after induction of anaesthesia with a laryngeal mask airway and the patient underwent a second stereotactic planning scan. Following intubation and induction of general anaesthesia, the operative wound was re-opened and the previously inserted Ommaya reservoir removed and this time a *modified Seldinger technique* was used to place the intracranial catheter.

The Backlund spiral biopsy needle was inserted and the spiral tip used to perforate through the firm capsule into the cyst. Once placement of the outer cannula within the cyst was verified by drainage of typical craniopharyngioma fluid, a guide wire was inserted into the cyst and the cannula then withdrawn. A small transverse incision was made in the distal tip of the catheter which was then passed over the guidewire, which was easily withdrawn once the catheter was positioned within the cyst.

Course: Postoperatively the patient experienced marked diabetes insipidus requiring regular DDAVP. He was reviewed by the radiotherapy service who felt him to be a good candidate for bleomycin; a contrast cystogram showed no evidence of a leak and accordingly he received his first dose of bleomycin without ill-effect.

He received a total dose of 44mg bleomycin following which the tumour size remained stable for

four years before showing progression, at which time he underwent radiotherapy. Visual acuity on the left had been poor at the outset and this gradually deteriorated to blindness; this may have been a complication of bleomycin as this occurred without any evident increase in the size of the tumour.

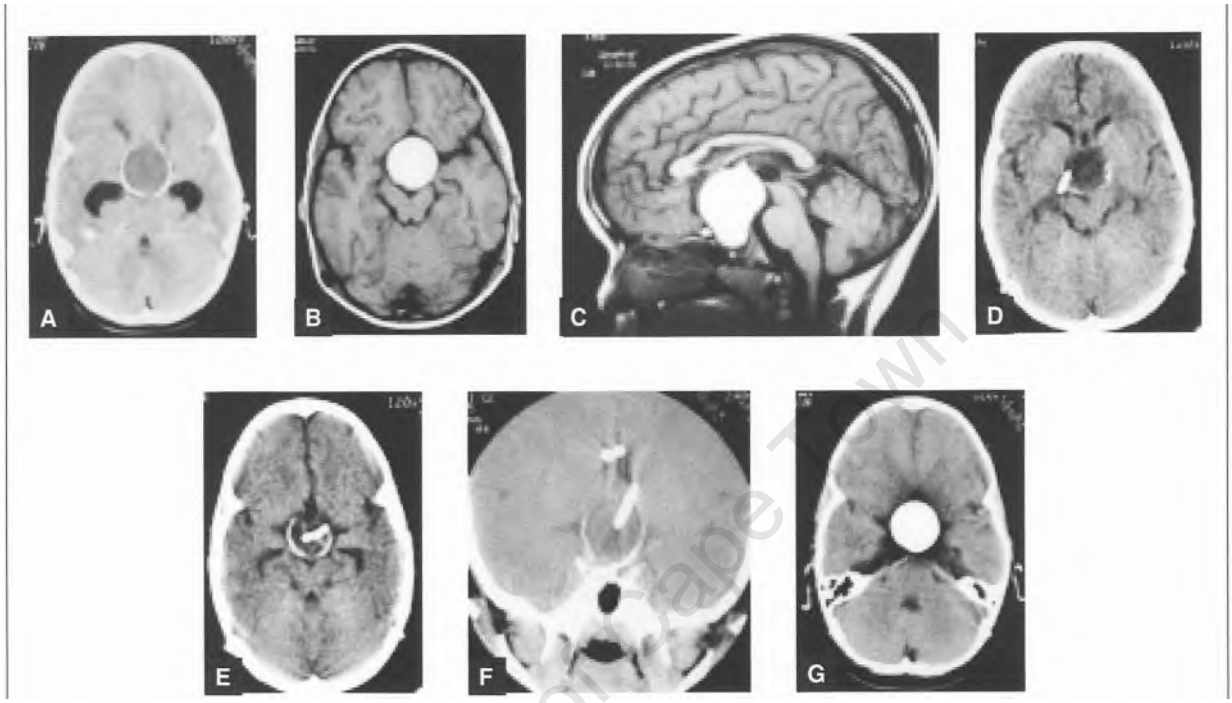


Figure 5.9: Initial CT scan showing a suprasellar cystic tumour with a densely calcified wall and accompanying hydrocephalus (a). Axial (b) and sagittal (c) T1 weighted MRI scans confirming extension from the sella into the third ventricle. CT scans after each of the two stereotactic operations showing the catheter alongside the cyst after the 1 ◦t operation (d) and within the cyst after the 2"d (e), confirmed on a corona! reconstruction (f) and contrast cystogram (g).

Problem:Surgical technique: unable to penetrate thick calcified cyst wall with stylet-containing catheter alone.

Solution:*Modified Seldinger technique,* using Backlund spiral biopsy needle to penetrate the through the wall, introducing a J-wire and railroading the fish-mouthed silastic catheter over this into the cyst.

Case 67

A 14 year-old boy presented with headache 6 months after undergoing thoracic laminectomy for debulking of a spinal cord astrocytoma. CT scan showed hydrocephalus with an enhancing lesion in the fourth ventricle and a smaller lesion in the left frontal horn. Stereotactic biopsy of the lateral ventricle mass was attempted via left frontal burr-hole; CSF was aspirated and histology of the small biopsy fragment showed choroid plexus.

Course: The patient underwent insertion of a VP shunt and a posterior fosse craniectomy for debulking of the tumour, following which he was referred for craniospinal radiotherapy.

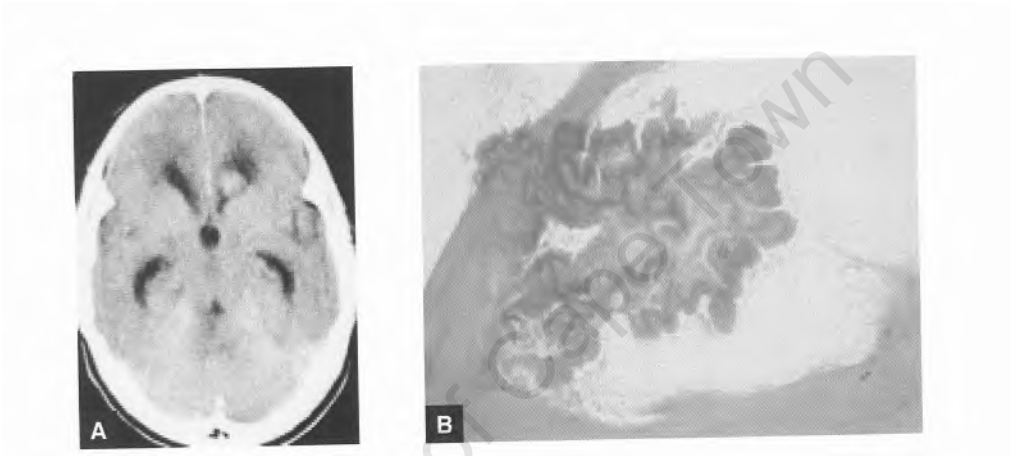


Figure 5.10: Axial CT scan showing enhancing lesion in left frontal horn (a); stereotactic biopsy was non-diagnostic, showing normal brain and choroid plexus (b).

Problem: Poor surgical decision, it is technically difficult to target intraventricular lesions using stereotaxis

Solution: Such a lesion is better approached using an endoscopy, which was introduced into our service the following year.

Case 75

A 32 year old female presented with right focal seizures of three weeks duration and had a past history significant for pulmonary tuberculosis treated five years ago. CT scan demonstrated a low-density ring-enhancing mass adjacent to the falx in the left parietal region; the differential diagnosis was thought to include an abscess or metastasis.

Stereotactic biopsy was attempted via a left parietal burr-hole; histology showed numerous eosinophils and neutrophils, which was interpreted as the capsule of an inflammatory lesion. A follow-up CT scan 24 hours after surgery showed an obvious tract leading to the edge of the lesion.

A repeat stereotactic biopsy was performed one week later; a more anterior entry point was selected and the previous burr-hole enlarged with a small strip craniectomy. Macroscopically the tissue obtained at biopsy resembled old blood clot and histology showed thrombus but no other pathological tissue.

Following surgery the patient recovered fully and was admitted to the Neurosurgical ICU with GCS 15/15 but she suddenly deteriorated after two hours, at which time CT scan showed a massive intracerebral haematomas necessitating immediate craniotomy. Copious tissue was sent to the pathologists but still no diagnosis could be made.

Course: The patient had a dense right hemiparesis which substantially improved over the course of three months. Follow-up CT scan showed no residual lesion and an angiogram was negative; a follow-up MRI scan was scheduled for six months and curiously this showed a *new* enhancing occipital lesion.

Craniotomy in July 1999 disclosed a *meningothelial meningioma* which was totally excised.

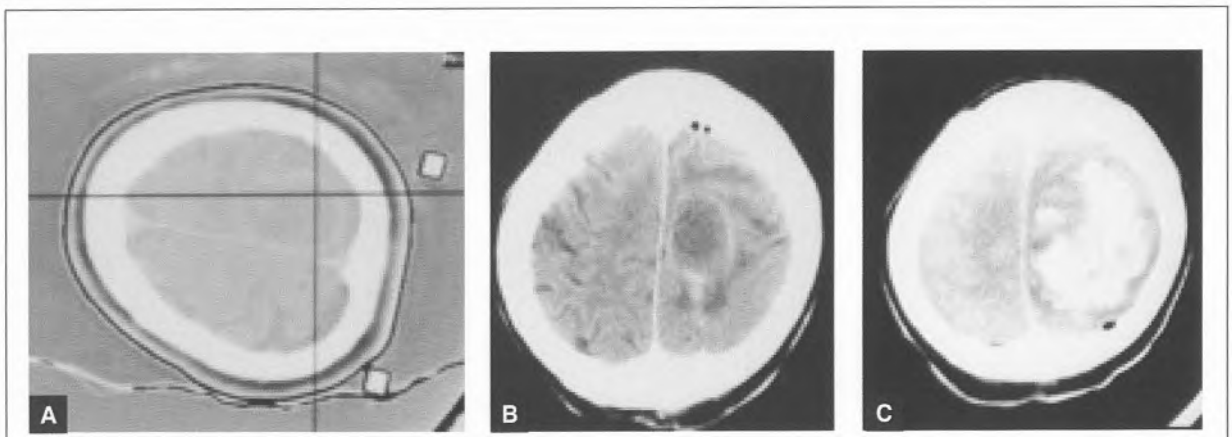


Figure 5.11: Axial CT scan showing the lesion on the first stereotactic planning scan (a); following a non-diagnostic biopsy, a thin tract is seen leading to the edge of the lesion (b). CT scan obtained urgently following the patient's abrupt deterioration 2 hours after a second stereotactic biopsy showed a massive intracerebral haematoma (c)

Problem: Poor biopsy technique. Despite the fact that no lesion was found at the time of craniotomy, it is likely that this was simply missed and non-representative tissue had been obtained at the time of stereotactic biopsy, due to not penetrating the lesion adequately.

Solution: Improved biopsy technique.

Case 77

A 29 year-old female presented with right sided weakness of four months duration on a background of headache for six months. CT scan showed an inhomogenously enhancing lesion in the genu of the corpus callosum with extensive low density in the frontal lobe.

- Stereotactic biopsy via a left frontal approach simply showed evidence of oedema in the white matter.

- A follow-up stereotactic biopsy one week later showed features of a high grade glioma on smear but this was not confirmed on the paraffin sections.

- A third stereotactic biopsy was performed and this confirmed a grade III astrocytoma; a titanium marker was left in place but this was not visible on the postoperative CT scan.

Course:The patient was referred to Radiotherapy for further management.

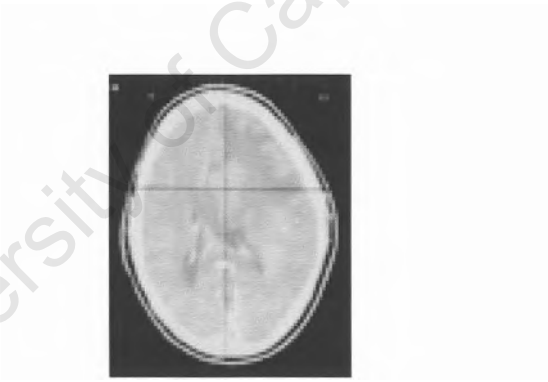


Figure 5.12: Axial CT scan demonstrating the target used for the third stereotactic biopsy.

Problem:Avoidable system error, lesion missed on the first biopsy and it is likely that only the edge was biopsied at the second operation as not all specimens were pathological. Surgical planning for the third biopsy was appropriate in targeting the *centre* of the lesion. This was the first case operated with the production version of the CTSP. In hindsight, it was realized that the calibration data on the software had not been changed from that of the prototype, hence this data was incorrect for this particular phantom and tripod.

Solution:Check every step of the procedure and all components when failure occurs. The success of the third biopsy was fortuitous as the problem had not yet been identified.

Case 78

A 6 year-old girl presented with a one month history of headache and vomiting on a background of longstanding polydipsia and short stature. CT scan showed a lesion typical of craniopharyngioma and a decision was made to treat her with bleomycin and implantation of an Ommaya reservoir was required.

In view of the patient's young age, the halo was attached under General Anaesthesia and the stereotactic scan was done under optimal circumstances and therefore highly accurate (maximum error 0.7mm). The surgical plan was to utilize the modified Seldinger technique we had developed, approaching the cyst via a right frontal approach avoiding the ventricle. This was challenging as the cyst was not particularly large (volume = 3.1 ml) and was vertically orientated, occupying the third ventricle. For the first time in this series, the Image Intensifier was utilized [Duffill], in order to visualize the tip of the guide wire to ensure that this did not penetrate into the subarachnoid space when utilizing the modified Seldinger technique.

When the catheter was passed under screening, it was seen to deflect off the shunt catheter, which quite clearly indicated deviation from the planned trajectory. This was attempted a second time and on further passage of the catheter, it appeared that the tip of the catheter was anterior to the sella and hence anterior to the tumour cyst. Clear fluid resembling CSF was obtained on gentle aspiration, confirming misplacement.

An attempt was made to re-insert the catheter after re-setting the phantom with a new target one cm more posterior, but this also failed to locate the tumour cyst. A decision was made not to leave a catheter in situ.

Course: The patient underwent craniotomy and subtotal resection of the tumour two weeks later and was subsequently referred for Radiotherapy.

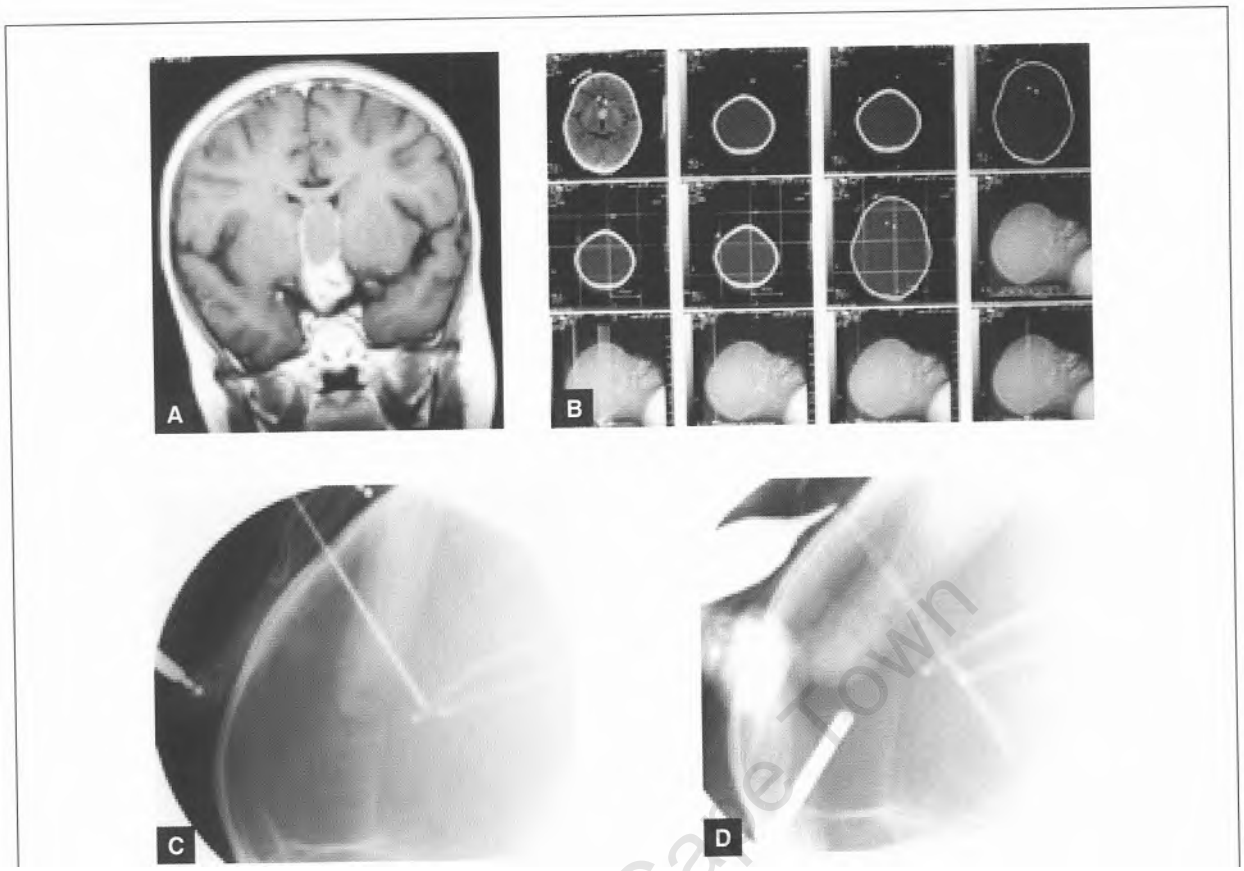


Figure 5.13: Corona! MRI showing the typical appearance of a mixed solid-cystic craniopharyngioma (a) and the stereotactic planning scan (b). Upon inserting the catheter stereotactically with additional fluoroscopic control, it was clear that the trajectory was incorrect. As can be seen in (c), the catheter displaced the tip of one of the shunts; the halo and two of the feet of the tripod can just be identified in this image. Upon reinserting the catheter, the trajectory appeared to be directed anterior to the sella and therefore anterior to the suprasellar cyst (d).

Problem: Avoidable system error. This was the first case operated at Red Cross Children's Hospital using the new production version and it was not initially understood why this problem had arisen.

Solution: Prior to doing the next paediatric case (Case No 80), the entire CTSP sequence was reviewed step by step by two of the Neurosurgeons (AGF and GAW) as it as apparent that there was a systematic error as similar problems had occurred at Groote Schuur Hospital (Case No 79).

In doing this, it was realized that the calibration data for the phantom and tripod had not been amended and we were using the new apparatus with the calibration data for the original prototype.

Case 79

A 52 year old female presented to a peripheral hospital with weight loss, confusion and incontinence of six months duration on a background of NIDDM and pulmonary tuberculosis. On examination she was mute with frontal release signs and a mild left hemiparesis. Investigations included HIV serology (negative) and lumbar puncture (0 polymorphonuclear cells, 3 lymphocytes, protein 0.83, globulin +). CT scan showed a faintly enhancing lesion in the medial right frontal lobe; the patient was commenced on 4-drug tuberculosis therapy and referred to Neurosurgery for consideration for biopsy of the intracranial lesion.

- Stereotactic biopsy via a right frontal approach was non-diagnostic, yielding degenerate neurons and perivascular gliosis, consistent with a "neighbourhood reaction". A postoperative CT scan the following day revealed a small haematoma anterior to intended biopsy site.

- A second biopsy one week later showed numerous reactive astrocytes but no inflammatory cells, necrosis or neoplasm. A follow-up scan showed a small locule of air lateral to the frontal horn, even further from the region of interest.

- A third stereotactic biopsy was performed two weeks later (21 days after the first biopsy) and this was also non-diagnostic, showing oedematous changes only.

Course: As no diagnosis had been made despite three attempts at biopsy, an opinion was sought from Neurology. Fine needle aspiration biopsy of a small lesion in the left upper lobe of the lung was recommended and this yielded acid-fast bacilli. The patient was continued on her course of 4-drug tuberculosis treatment and transferred to a convalescent care facility, but her condition did not improve and she died two months later.

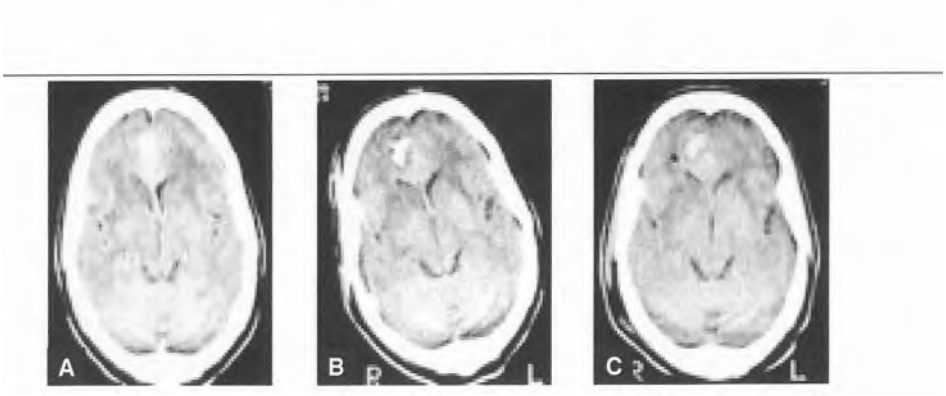


Figure 5.14: Axial CT scan showing the faintly enhancing lesion in the medial right frontal lobe (a); the site of the first stereotactic biopsy was clearly incorrect, as shown by the small haematoma anterolateral to the mass, and the second biopsy was even more lateral (c). A CT scan was not requested after the third biopsy.

Problem: Avoidable system error with the first and second attempts.
Possibly this patient had an inflammatory process not amenable to diagnosis by stereotactic biopsy, as the third biopsy was performed after correcting the calibration data.

Solution:With the exception of the third biopsy in this patient, correction of the calibration data appeared to address the system error as no further targeting problems were encountered in this series.

Case 80

This 13 year old boy was referred to Ophthalmology with a history of headache and visual symptoms noted at school over the past month. He had a right temporal hemianopia and disc pallor; CT scan showed a suprasellar predominantly cystic lesion typical of craniopharyngioma but no hydrocephalus. He had delayed puberty and endocrine workup confirmed hypopituitarism; a decision was made that l he would best be managed with intracystic bleomycin.

- The halo was attached and the stereotactic planning scan performed under anaesthesia with a laryngeal mask airway, following which he was intubated for surgery. Two attempts were made to introduce the catheter with the thin stylet in place but the tip felt as though it was being deflected by the mass. The Backlund spiral biopsy needle was then introduced with the intention of using the modified Seldinger technique but the needle abutted against the proximal end of the standard instrument guide before it entered the cyst. The needle was therefore removed and the instrument guide replaced with the cutoff guide to enable deeper intracranial penetration. A definite "give" was felt when the needle was inserted beyond the depth of the capsule but torrential arterial bleeding ensued when the stylet was removed, indicating a significant vascular injury.

  A decision was made to proceed immediately with a pterional craniotomy; the needle had been left in place to enable ongoing decompression of the haemorrhage and this was replaced with a silicon ventricular catheter when the craniotomy was performed. Upon opening the dura the brain was not unduly tense and as there was no active bleeding, no further exploration was attempted.

  The bone flap was left out and an urgent CT scan showed extensive subarachnoid haemorrhage and the patient was admitted to the Neurosurgical ICU for ventilation under propofol sedation.

  He was weaned and extubated after 48 hours at which time he had a dense left hemiparesis. Angiogram showed no evidence of a false aneurysm or other vascular injury.

- A decision was made that treatment with bleomycin remained the fist choice for him and he therefore underwent a second stereotactic procedure, with the catheter being inserted uneventfully on this occasion. He experienced diabetes insipidus after this operation and remained in ICU for 8 days postoperatively, before being fit for transfer to the Paediatric ward.

Course:The patient received a total of 32 mg of bleomycin, following which the cyst remained stable for 3 years, at which time progression was treated with Radiotherapy. Further enlargement of the intrasellar cyst was managed by transsphenoidal surgery and later subfrontal decompression.

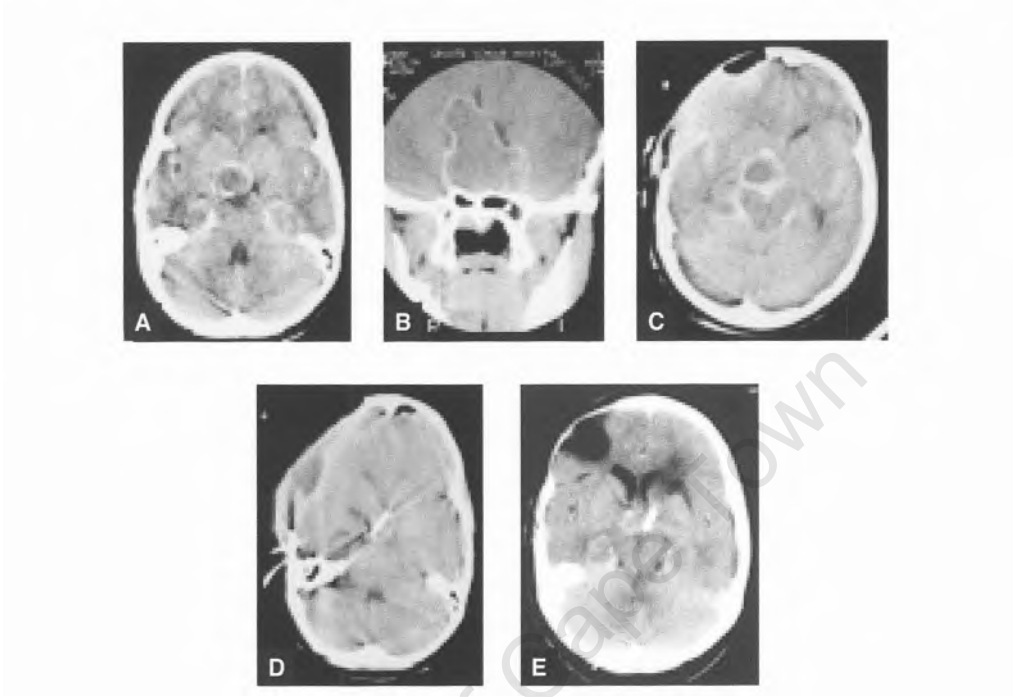


Figure 5.15: Initial axial CT (a) and reconstructed corona! CT (b) showing the enhancing thick tumour cyst wall; immediate postoperative CT showing extensive subarachnoid haemorrhage (c). CT Scan following 2" operation, confirming intracystic placement (d). Follow-up CT five months later, showing low density change along catheter as well as right frontal porencephaly underlying the cranial defect (e).

Problem:Surgeon error in attempting to penetrate cyst wall using the blunt tip of the biopsy needle and not the spiral.

Solution:Introduce spiral tip of needle using corkscrew action to enter the cyst.

5.13 Perspective

The results reported here reflect two simultaneous processes- a new stereotactic system was being developed, by surgeons who were also learning the principles of stereotaxis. Other authors have commented on the increased rate of errors when using a prototype [Gumprecht] and in the early phases of introducing a production version into practice [Heilbrun_1983]. It is also clear that there is a learning curve in introducing stereotactic techniques [Barnett 1999].

Very few publications reporting a series of stereotactic procedures specifically present the distribution of volumes, but the lesions operated on in this series tended to be small as large lesions were operated on "freehand".

Apart from two targeting errors early in the series, both of which led to fundamental changes, most of the errors represented incorrect surgical decisions, while the high number of inconclusive biopsies early in the series could be ascribed to a number of reasons, as will be discussed in the next chapter. The sequence of failed procedures spanning the transition from the prototype to the production version was due in a sense to the CTSP becoming a victim of its own success in that a number of surgeons were using the system independently by that stage and it therefore took time for the developers to realize that there was a problem.

The 115 operations reviewed in this chapter will now be reviewed in terms of the procedures performed, encompassing stereotactic biopsy in the next chapter, stereotactic chemotherapy in Chapter 7 and a range of other clinical application in Chapter 8.

Chapter 6

Stereotactic Brain Biopsy

6.1 Introduction

By far the commonest indication for morphological stereotactic surgery is retrieval of tissue specimens for diagnostic purposes. An oft-cited study found that 12% of patients undergoing stereotactic biopsy at a major academic institution were found to have diagnoses that were not considered prior to surgery [Friedman_1989]. While the greatest experience with stereotactic tumour biopsy has emanated from such centres, the value of this technique to all neurosurgeons in practice is borne out by a series in which stereotactic biopsy led to a change in management in 40% of cases in a community hospital setting [Plunkett].

Early applications of stereotaxis were directed at the treatment of tumours by implanting various isotopes, while the use of this approach for biopsy alone appears to have lagged [Dagi]. This was due largely to deficiencies in the methods available for delineating such lesions and then retrieving pathological tissue. An atlas could be used to guide functional procedures, but was of little help in dealing with conditions such as intracerebral tumours where normal anatomy was inevitably altered. The presence of a lesion had to be deduced indirectly from features such as ventricular displacement or a vascular blush; Talairach's group tackled this problem with particular vigour, utilizing angiography to devise the system of *repérage* [Kelly 2004i].

A technique for tissue retrieval from deep brain structures at the time of functional stereotactic surgery was described in 1964 [Kalyanaraman]; the authors demonstrated that this could be done safely, in performing 155 biopsies in 65 patients. They speculated that their method could be applied to deep-seated brain tumours and this was confirmed nine years later when 28 patients, out of a series of 31 reported, had a diagnosis made with this technique using the Todd-Wells stereotactic apparatus [Conway]. The challenges of preoperative imaging were immense at that time- patients underwent a selection of skull x-rays, angiography, pneumoencephalography, positive contrast ventriculography and radioisotope scans!

The advent of CT scanning the same year [Hounsfield] had an immediate impact on neurosurgery. An ingenious technique for CT-guided biopsy of intracranial lesions was reported as early as 1977 [Maroon]; the original EMI scanner required the patient's head to be immersed in a water bath and this presented substantial challenges in performing a neurosurgical procedure!

There was however another reason for the limited application of stereotactic techniques to brain tumours during the pre-CT era. As many intracranial tumours presented only once they exerted mass effect, needle biopsy in these patients with critically raised intracranial pressure carried a high mortality as a minor degree of haemorrhage could prove critical. Biopsy could also provoke brain swelling which was very difficult to control prior to the availability of steroids. The outlook for glioblastoma was dreadful, with operative mortality as high as 40% following needle biopsy [Frankel].

In light of these concerns, craniotomy was preferred for diagnostic purposes in North America, while needle biopsy was often used in Britain. Prior to using a stereotactic technique, needle biopsy was performed "freehand" with a diagnostic yield that varied between 33% and 88%; this was dictated in part by the diameter: depth ratio of the lesion [Lee]. Following the introduction of CT-guided stereotactic biopsy at two British centres, the diagnostic yield increased from 64.9% for freehand biopsy to 92.1% for stereotactic biopsy, accompanied by an improvement in the operative mortality from 5.5% to 1.3% [Lee]. Although some centres reported disappointing results with stereotactic approaches compared with freehand CT-guided techniques [Wen], cumulative experience eventually settled this debate.

In the current era of "frameless stereotaxy", it is worth remembering that stereotactic frames didn't only bring a new level of accuracy, but also a novel degree of stability in that the needle was passed along a single trajectory. The instrument was therefore prevented from moving erratically from side to side and this may well have been an important factor in reducing morbidity.

At the other end of the resource spectrum, it is salutary to reflect that freehand approaches to such lesions are still practiced by neurosurgeons who do not have access to any stereotactic equipment at all. Although this may still be a reasonable therapeutic strategy when approaching a large lesion such as an abscess, it is not at all ideal for retrieving a diagnostic sample.

6.2 Aims of stereotactic biopsy

The aim of stereotactic biopsy is to retrieve a sample of abnormal brain tissue for analysis by the pathologist in order to make a definitive diagnosis; this specimen must be representative of the pathological process and sufficient to allow adequate histopathological examination. As this is seldom a therapeutic intervention in its own right, the procedure must be performed safely.

6.3 Indications

Before embarking on a stereotactic biopsy, certain requirements must be met:

i. A lesion can be seen on imaging

As the essence of stereotactic surgery is the careful selection of a target, there must be a focal lesion that can be defined in three-dimensional space, not only on the patient's initial imaging study but also on the imaging to be used to plan the biopsy. Intravenous contrast may need to be administered in order to define the lesion, or to refine the choice of target.

ii. The diagnosis cannot be established *non-invasively*

A time-honoured dictum in neurosurgery is that one cannot make a diagnosis of an intracranial mass without examining part of that lesion under the microscope. However, with the ever-improving diagnostic capabilities of modern imaging, ranging from MRI, including MR spectroscopy, though to PET, one may well be able to make a diagnosis without recourse to an invasive procedure. An example of this is the relatively common paediatric entity of a pontine glioma, where there is now common agreement that the characteristic low-intensity expansion of the upper brainstem together with encasement of the basilar artery make any other diagnosis so unlikely as to render a tissue diagnosis unnecessary for routine clinical practice.

Other scenarios include patients with systemic conditions such as HIV, where serological tests or even a trial of therapy may point to the nature of the intracranial lesion, or the patient who presents with an intracranial mass that appears most likely to be a metastasis with lesions elsewhere; in this case, less invasive strategies, such as bronchoscopic biopsy should there be a lung lesion, may be sufficient.

iii. A more definitive option is *not* available

Stereotactic biopsy is ideal for small lesions in eloquent areas, or for multiple lesions, but may well be contra-indicated in the patient with a very large tumour with raised intracranial pressure. Such patients are very susceptible to even minor procedures; although the volume of the needle is negligible and does not itself cause a problem, its passage through the brain may cause additional swelling or the biopsy may result in a haemorrhage which critically increases intracranial pressure. In such a patient it is usually preferable to perform a craniotomy and partially debulk the mass even if the

goal is not total excision. An exception may be a patient who is too unwell to tolerate a craniotomy but a diagnosis is nonetheless considered mandatory.

The emergence of other minimally invasive techniques has also impacted on surgical decision-making, such as the use of neuro-endoscopy for lesions such as colloid cysts and pineal tumours.

iv. A vascular lesion is excluded

Haemorrhage is the most feared complication of stereotactic biopsy and lesions such as giant aneurysms, arteriovenous malformations (AVM) or cavernous angiomas are absolute contra-indications to this technique. Suggestive features would include the pattern of enhancement and the location, hence adequate imaging should deter stereotactic biopsy in such cases; cavernous angiomas usually have a characteristic appearance on MRI and angiography should identify aneurysms and AVMs. Some of the pre-MRI stereotactic series reported attempts to biopsy these with adverse consequences.

In a similar vein, in planning any stereotactic biopsy it is vitally important to be able to access the lesion without having to traverse areas of high vascularity such as the Sylvian fissure.

v. There is no contra-indication to surgery

All the usual standard considerations apply:

- **Coagulopathy**

  The issue of intracranial haemorrhage after stereotactic biopsy is addressed below, but two factors that significantly increase the risk of a haemorrhage complicating needle biopsy of the brain are a bleeding diathesis or uncontrolled hypertension. Stereotactic biopsy should be avoided in patients who have been using aspirin, although it is less clear that the same risk attends the use of other non-steroidal anti-inflammatory agents.

- **Local sepsis**

  Any infection involving the scalp, skull or subdural space in the vicinity of the surgical site greatly increases the risk of intracranial sepsis as a complication.

- **Terminal illness**

  Patients who are critically ill or have very advanced disease with a poor performance status (e.g. low Karnofsky score) may not benefit from histological confirmation that they do indeed have a high grade glioma.

In summary, stereotactic biopsy is most commonly indicated for lesions which are:

- Deep
- In eloquent brain regions
- Multiple
- High risk for another approach

Stereotactic approaches are not indicated when a large tissue sample is required, such as with diagnostic brain biopsy for elusive neurological conditions [Kaufman].

6.4 Biopsy instruments

Just about every different type of stereotactic frame that has been manufactured has been used to perform a biopsy.

The main area of contention is the instrument used to retrieve the specimen. The first needle used for this purpose was a hollow cannula with a hole at the distal end and a central stylet. To the dismay of the neuropathologist, brain samples aspirated using such needles are usually somewhat disrupted and a variety of other instruments have been devised. These entailed either guillotine-like excision of a piece of the lesion or grasping a specimen with a cup forceps.

i. **guillotine-type action**
   - end-on *Backlund spiral needle*
   - side-cutting *Sedan, Nashold needle*

ii. **small cupped forceps**
   - microforceps *Gildenberg forceps*

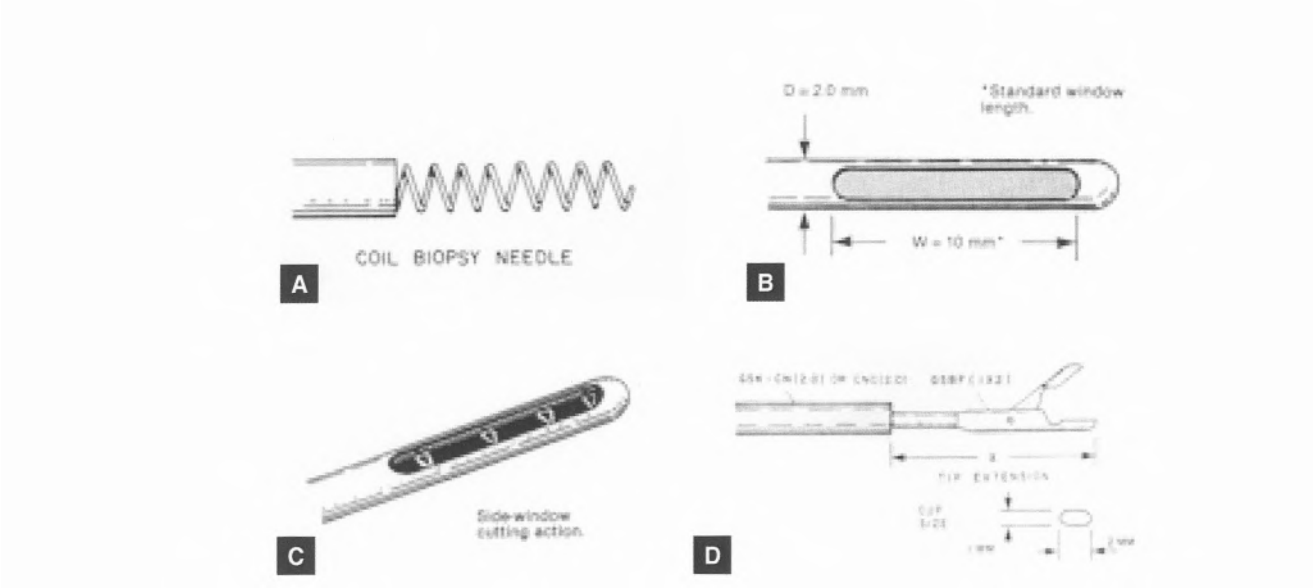


Figure 6.1: Stereotactic biopsy needles; various modifications of each of these have been introduced. The spiral or coil needle (a) should be introduced into the lesion with gentle rotation and the biopsy is then taken by sliding an outer cannula over the corkscrew. Perhaps the most popular is the side-cutting needle which consists of two cannulae, one inside the other, each with a window 10mm in length (b). The needle is introduced with the outer window "closed" and this is opened with a simple rotatory action, a sample is aspirated with gentle suction at the proximal end and retained by closing the window (c). Some prefer using microcup forceps as this may give more refined haptic feedback from the lesion (d). (Figures from [Cosman], with permission from Wolters Kluwer)

The inventive Swedish neurosurgeon Erik-Olof Backlund, frustrated by the difficulty of biopsying craniopharyngiomas, designed a spiral biopsy needle which has been widely used [Backlund_1971]. The principle entails rotating the tip into the tumour in a corkscrew fashion and then sliding the outer cannula over the spiral, coring out a specimen 10 mm by 1-2 mm. Paradoxically this was found to be good for soft tumours such as gliomas but less effective when there was a firm capsule.

The most commonly cited choice however is a side-cutting needle; this is essentially a suction biopsy device. There are different sizes available, but it seems most authors favour a needle 2.1 to 2.5mm in outer diameter that produces a core that is 5 to 10 mm by 1.5 to 2 mm in size. Lunsford credits Professor Sedan in Marseilles with the introduction of this instrument, although others have subsequently described modifications; in his view, use of this needle cuts the risk of haemorrhage by 75% [Lunsford_2002].

Other workers advocate the use of a small cupped biopsy **forceps** such as used for bronchoscopic biopsies, because there is more refined haptic feedback or "feel"; it has been suggested that this enables the surgeon to know when s/he has grasped a vessel as this imparts greater resistance [Cook]. The specimens are usually significantly smaller than with other instruments, usually around 1.5mm^3 in size.

Some authors have voiced strong opinions as to the relative merits of the different instruments and there also appear to be regional preferences, but it has been pointed out that there is no evidence upon which to base claims on this matter as no prospective study has been conducted to determine the best technique [Kulkarni_1999]. Some surgeons who have used a variety of different biopsy instruments have concluded that complications are equivalent [Thomas_1989]. As with most surgical nuances, the best strategy is for the neurosurgeon to use whichever technique s/he is comfortable with.

6.5 Medical management

- **Antibiotics**

  In this series, prophylactic antibiotics were administered in 67.8% of the procedures overall but in only 52.1% of the biopsies. Following local practice guidelines, the antibiotic given was as a single dose at induction of anaesthesia, most commonly 1g intravenous cefazolin in adults or 50mg/kg intravenous cloxacillin in children. Of the two surgeons who performed the majority of the procedures, one favoured the use of prophylactic antibiotics while the other did not, with no discernible difference in the risk of surgical site infection.

  Only one septic complication occurred in this series, with local wound sepsis developing in a patient in whom a brain abscess was tapped; this patient had already been commenced on therapeutic doses of intravenous antibiotics one week prior to surgery.

- **Steroids**

  Use of steroids such as dexamethazone in the setting of perilesional cerebral oedema is advisable; of patients undergoing stereotactic biopsy in this series, 82% received intravenous dexamethazone prior to surgery and the usual practice was to continue this for a short period thereafter.

The patient whose death 4 days after biopsy was considered to be a consequence of exacerbating pre-existing raised intracranial pressure (Case 72), had been on an adequate course of steroids before and after surgery. All of the patients who manifested a transient worsening of their neurological status, either leg weakness or dysphasia, had also received steroids.

Anticonvulsants

Intraoperative seizures are uncommon during stereotactic biopsy and did not occur in our series, probably because 96.5% of patients received general anaesthesia. Seizures had been a presenting symptom in 30% of the patients in this series and consequently a number of patients had been commenced on therapeutic anticonvulsants. The place of prophylactic anticonvulsants is less clear; 57.4% of patients in this series received anticonvulsants while 66% of those undergoing biopsy did so. Local practice was to use phenytoin for this purpose and it is noteworthy that the commonest minor complication in this series was skin reactions to this drug, which occurred in seven cases.

6.6 Anaesthetic management

Stereotactic biopsy can be performed without general anaesthesia, provided the patient is able to cooperate fully and effective local anaesthesia is used. Local preferences certainly play a role- it has been noted that most procedures in the UK were performed under general anaesthesia, while in Australia, Europe and North America local anaesthesia was preferred [Bradburn]. Some patients, in particular young children and confused or frightened adults, and certain operative interventions, such as posterior fossa procedures in the prone position, require general anaesthesia.

In all adult cases in this series, the CTSP halo was applied without recourse to general anaesthesia; oral analgesia and sedation was typically administered in the ward prior to infiltrating local anaesthesia with a vasoconstrictor (usually 1% lignocaine with 1:100,000 adrenaline, using a dental syringe).

Most children underwent general anaesthesia, often with insertion of a laryngeal mask airway (LMA), prior to applying the halo. The disadvantage of applying the halo in the Operating Theatre is that portable monitoring has to be available for safe transfer to and from the CT scanner. With many conventional stereotactic frames, there is potential for the frame itself to hinder access to the airway [Bradburn]. This is not an issue with the CTSP

As with colleagues in the United Kingdom [Wild], Brazil [Ferreira] and Turkey [Calisaneller], our practice was to use general anaesthesia unless there was a particular contra-indication. One of the reasons for this was the fact that performing stereotactic surgery was a new experience for both the neurosurgeons and the anaesthetists, and seldom was the same anaesthetist in attendance. The small number of adults who underwent their stereotactic operation without requiring general anaesthesia (4.3%) tolerated this well and none of these cases had to be aborted.

If the case is done without general anaesthesia, it is important that this be borne in mind by everyone in Theatre, especially in discussing the provisional pathological diagnosis within the room and over an intercom. There was no better illustration of this than one of our cases where the patient undergoing biopsy of an intracranial metastatic adenocarcinoma was a retired technologist from our own Pathology laboratory.

6.7 Biopsy procedure

By convention, all intracranial access in our department has been via a burr-hole and a twist drill has not been used; naturally this was also our approach to performing stereotactic biopsies, but it is clear that many experienced neurosurgeons prefer using a twist drill. Although a burr-hole has the theoretical advantage of enabling visualization of the cortex, and therefore enables the surgeon to avoid any surface vessels, in reality the complication rate with a twist drill is remarkably low [Maartens].

As previously discussed, various different biopsy needles are available. Taking more than one biopsy sample increases the yield [Aker], but limiting the number of needle passes though the brain reduces morbidity. Most biopsy needles are designed such that they have an outer sheath that can be left in place while an inner cannula containing the tissue sample is withdrawn. Should one use the side-cutting needle, taking biopsies with the window facing in different directions is recommended [Fritsch].

Often pathological tissue has an abnormal appearance in terms of colour and consistency, but if there is any doubt the neurosurgeon is well advised to await an intraoperative smear. In the course of this series the pathologist was seldom present in the operating theatre; biopsy specimens were placed on a glass slide which was immediately transported to the pathology laboratory in an airtight container without any fixative. A smear was done in the majority of cases; tissue for definitive histopathology was embedded in paraffin and stained with haematoxylin and eosin

(H&E), with further studies such as immunohistochemistry or other special stains performed as indicated.

If there was any suspicion of infection, separation of specimens for routine microscopy, culture and sensitivity, Ziehl-Neelsen stain and TB culture and fungal culture is best done sterile in the operating theatre, rather than in the pathology lab.

6.8 Postoperative management

The main objective in caring for these patients after surgery is to detect the onset of a neurological deficit as a manifestation of haemorrhage or swelling. The major controversies relate to two issues:

- should patients undergo routine imaging immediately after surgery?
- should patients should undergo postoperative observation in an Intensive Care Unit (ICU), and for how long?

The one patient in this series who developed a significant intracerebral haematoma that required craniotomy for evacuation deteriorated abruptly two hours after surgery; this complication manifested with deterioration in the patient's level of consciousness, as assessed by the Glasgow Coma Score (GCS) [Jennet]. Neurological observations in the ICU sufficed to detect the problem in this instance and this was confirmed by a CT scan (Figure 6.2).

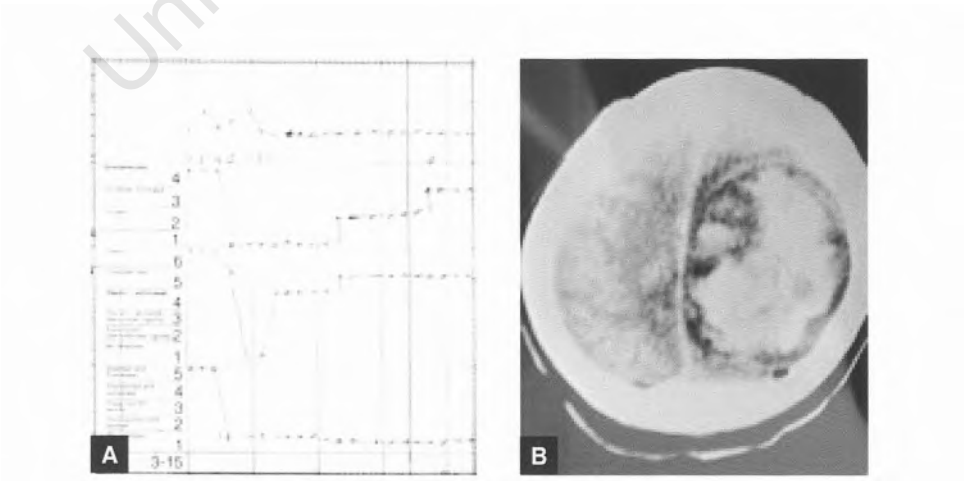


Figure 6.2: Postoperative haematoma. An abrupt deterioration in the patient's level of consciousness, as indicated by a drop in the GCS from 15/15 to 7/15 (a) prompted an immediate CT scan which disclosed a postoperative haematoma (b).

The main reason to scan patients postoperatively is to detect a silent haemorrhage that may lead to sudden clinical deterioration. This complication will be looked at in greater detail later, but it is important to bear in mind that most haemorrhages occur at the time of surgery; although delayed haemorrhage has been described, occurring in 0,4% of cases in one large prospective series where patients had all undergone an intraoperative CT scan within 15 minutes of biopsy [Field], this is rare enough to not inform routine care. A study from the Cleveland Clinic noted that all haematomas manifested within 6 hours [Kaakaji], as is the case with neurosurgery in general [Taylor].

Our routine practice was to admit patients to ICU after stereotactic biopsy, but recent literature suggests that this may not be necessary. This is a very important consideration in our setting, where access to ICU is limited and procedures are often cancelled due to space not being available. The Cleveland Clinic study suggested that patients could be discharged home safely 8 hours after biopsy, provided the CT scan was reassuring [Kaakaji]. A further helpful study in this regard emanates from Toronto, where 73 patients out of a consecutive series of 75 ambulatory patients were safely discharged on the same day, after 4 hours of observation [Bhardwaj]. The sophisticated environment in which these colleagues practice certainly helped in that all patients were visited at home by a home care nurse that evening, a service that would be hard to imagine in our setting, but significantly, confidence in clinical parameters was demonstrated in that routine postoperative imaging was *not* part of the management protocol. This article was accompanied by seven editorial comments, ranging from enthusiastic to skeptical, suggesting that there is a wide range of opinions on this matter.

In order to ascertain the national practice pattern in the USA, Warnick surveyed active members of the AANS/CNS Joint Section on Tumors and found that 59% performed routine CT scans after stereotactic biopsy, particularly those surgeons not practicing in academic settings and also those surgeons who had been in practice for more than a decade [Warnick]. The authors developed an algorithm which was then validated by prospective implementation; this called for CT scanning and ICU admission only for patients who experienced intraoperative haemorrhage or manifest new neurological deficits. All other patients were monitored for 2 hours in the recovery room and then transferred to a regular ward.

6.9 Stereotactic biopsy in Special locations

The deeper, less accessible areas of the brain present particular challenges to the neurosurgeon and stereotaxis has much to offer in biopsy of lesions in the brainstem and pineal region.

6.9.1 Brainstem

The brainstem is perhaps the region where a stereotactic approach is most helpful, given the fact that intrinsic lesions are seldom amenable to radical resection. Extreme levels of accuracy are required, given the proximity of critical neural structures and the distance from the cranial surface coupled with the fact that these lesions are usually relatively small. Although the majority of brainstem masses are neoplastic, a wide array of other pathological conditions may also be encountered, particularly in developing countries where infectious lesions such as TB may present as isolated brainstem masses [Rajshekar 1997].

Case illustrations

Two patients who underwent biopsy of lesions in the upper midbrain, via a transfrontal approach, will be reviewed in detail.

Case 39

This 4 year old boy presented with left sided weakness which had progressed over one month. CT scan showed a mixed solid-cystic mass in the midbrain, extending into the right cerebral peduncle; the solid component enhanced avidly following intravenous contrast. As resection was indicated should this be a low grade neoplasm, a stereotactic biopsy was performed.

Following induction of anaesthesia and insertion of a laryngeal mask airway, the halo was attached in the Operating Theatre, positioned in the right frontal area to enable the burr-hole to be positioned just behind the corona! suture, two centimeters off the midline. The patient was transferred for the planning CT scan, breathing spontaneously with the AMA in place and once back in the Operating Theatre, he was intubated and ventilated. Two specimens were taken with a target in the solid component, using the side-cutting needle with the window directed medially and then laterally. In view of the depth of the lesion, the outer cannula was left in place between biopsies with only the inner cannula withdrawn to remove the specimen. The tripod was then reset for a second target within the cyst and 2m1 of deeply xanthochromic fluid was aspirated.

Course:Histology showed a pilocytic astrocytoma hence the patient underwent craniotomy and resection of the tumour via a right subtemporal approach. In view of the low grade histology he was not referred for radiotherapy but he presented one year later with hydrocephalus following tumour progression. A ventriculo-peritoneal shunt was inserted and he subsequently underwent two further resections, ultimately resulting in cure.

Comment: The initial biopsy was very helpful in that it demonstrated that this was a lesion amenable to radical resection. The patient is alive and well 12 years after diagnosis.

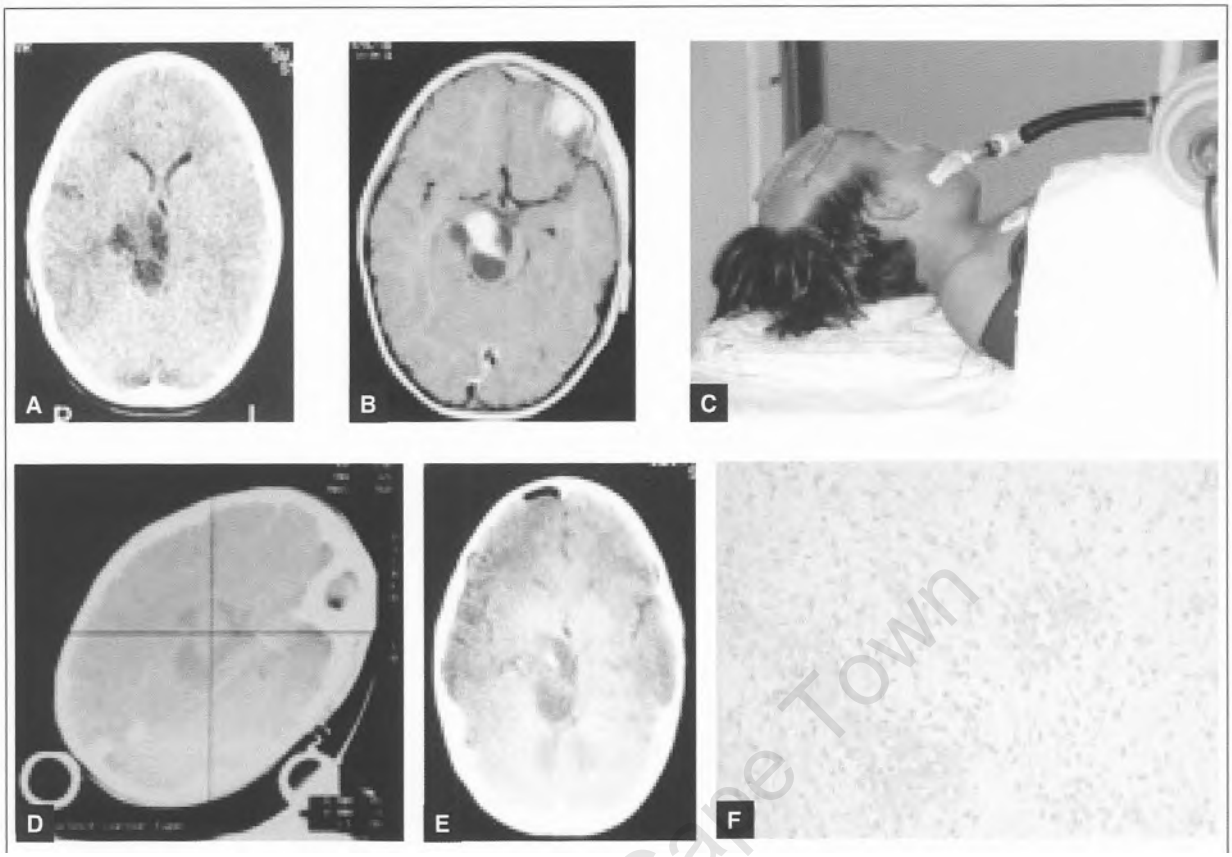


Figure 6.3: This mixed density lesion visible in the midbrain on CT scan prior to administration of intravenous contrast (a) enhanced avidly following contrast, well seen on axial Ti MRI (b). The patient underwent the planning CT scan breathing spontaneously with a laryngeal mask airway in place (c). A target was selected to the right of the midline (d) and a small haematoma is evident at the site of the biopsy on CT scan one day after surgery (e). H&E stain showed bipolar astrocytic cells and moderate vascular proliferation, typical of a pilocytic astrocytoma (f).

Case 40

This 16 year old girl presented with left sided weakness of two weeks duration, accompanied by swallowing difficulty and voice changes. Examination confirmed a mild hemiparesis with bulbar signs and nystagmus. Imaging showed a poorly defined lesion in the rostal midbrain and posterior thalamus on the right. As the lesion had a wide differential diagnosis, a stereotactic biopsy was performed.

This was performed in a similar fashion to the previous case, with initial insertion of an laryngeal mask airway for the duration of halo attachment and planning CT scan in view of the patient's young age, followed by intubation and ventilation for surgery. Two biopsies were taken at the same target, oriented in opposite directions with clearly abnormal mucoid tissue obtained.

Course: Histology disclosed an anaplastic astrocytoma hence the patient underwent a full course of craniospinal radiation. She returned 8 months later with worsening of her neurological status and was found to have a ring-enhancing lesion in the inferior right frontal lobe. A second stereotactic biopsy confirmed this lesion was also an anaplastic astrocytoma and the patient was referred back to the Radiotherapy service for further management.

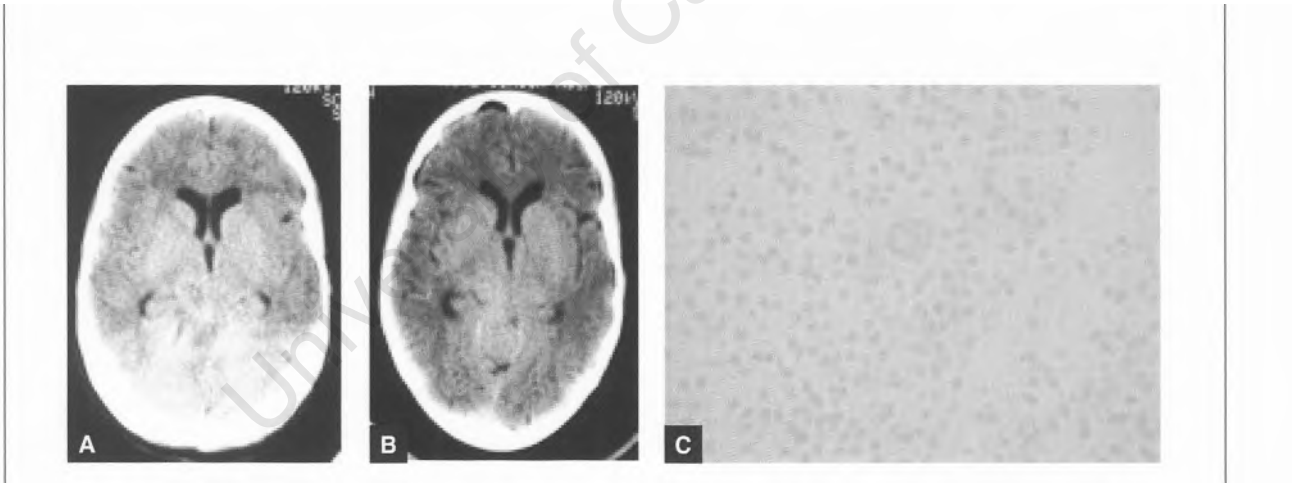


Figure 6.4: Axial CT scan demonstrating an indistinct lesion in the upper midbrain on the right, showing faint ring-enhancement (a); follow-up scan one day after surgery shows a very small haematoma at the site of the biopsy (b). Histology was characteristic for an anaplastic astrocytoma (c).

Comment: Stereotaxis enabled the focal brainstem lesion in this young patient to be diagnosed with certainty at presentation, facilitating appropriate management. When she experienced a recurrence, this could be confirmed without subjecting her to craniotomy.

Stereotactic trajectory

Prior to the advent of CT scanning, the diagnosis of a brainstem tumour was usually made on clinical grounds, occasionally supported by ventriculography. Surgical exploration was attempted in a minority of cases, but carried a dreadful mortality of up to 60% in this setting [Villani]. The first report of CT-guided stereotactic biopsy of a brainstem lesion was published 30 years ago; a Leksell stereotactic frame was used but no specific details of the approach were provided [Riegel 1979]. Following this, a number of neurosurgeons reported their experience, either as part of a larger series [Ostertag, Apuzzo 1983], or as a smaller series with a specific focus on the brainstem [Hood, Thomas_1988, Kratimenos].

A consensus developed that infratentorial lesions such as lesions in the rostra! brainstem could be approached safely via a supratentorial transfrontal stereotactic approach, allowing a trajectory directed thought the tentorial hiatus along the axis of the brainstem, while conversely the use of a supratentorial approach to the cerebellum, traversing the dura of the tentorium cerebelli, was fraught with hazard.

- **Ipsilateral transfrontal**

  Following Riegel's series, a case report described the successful management of a midbrain haematoma in a young medical student from Boston, utilizing transfrontal aspiration [Beatty]. Venes's group at Ann Arbor published a detailed account of their technique using intravenous contrast and reformatted coronal and sagittal images to plan the angle of the trajectory, as well as using stimulation at the target site prior to taking a biopsy in awake patients [Hood]. Apuzzo's landmark series contained 129 patients who underwent stereotactic biopsy of diencephalic-mesencephalic lesions [Apuzzo 1987].

  The early experience from Queen's Square using a precoronal burrhole [Thomas_1988] was followed up with a series of 72 patients [Kratimenos]. The entry point was typically just behind the coronal suture and 1-2 cm off the midline; a burrhole was recommended in order to visualize any bridging veins. Avoiding puncture of the tentorium was considered essential in view of the high risk of cranial nerve and vascular injury, but traversing the lateral ventricle appeared to have few complications.

- **Suboccipital transcerebellar**

  As mentioned, the tentorium precluded access to the cerebellum from a supratentorial approach although some authors described techniques for penetrating this [Apuzzo_1983].

Following an initial report from Pittsburgh [Coffey], an approach traversing the middle cerebellar peduncle was described in a series of 26 patients from the Mayo Clinic who underwent biopsy of a pontine lesion via a suboccipital approach [Abernathey]. This yielded a diagnosis in all patients with no complications, but a disadvantage was the need for general anaesthesia as the patient was prone.

Contralateral transfrontal

The inner margin of the tentorium may hinder the ipsilateral transfrontal approach to the midline via the incisura; a novel contralateral approach enables biopsy of lesions in the lateral pons and lateral cerebellar peduncle (Figure 6.5) [Amundson]. The burrhole is located about 4cm off the midline and a completely intraparenchymal trajectory is planned, avoiding the lateral ventricle and aqueduct, veins, arteries and tentorium. These cases are ideally operated on awake as this enables early detection of a neurological deficit [Shad]. Should the configuration of the target demand a transventricular route, this may be used without ill-effect [Pereira_2008].

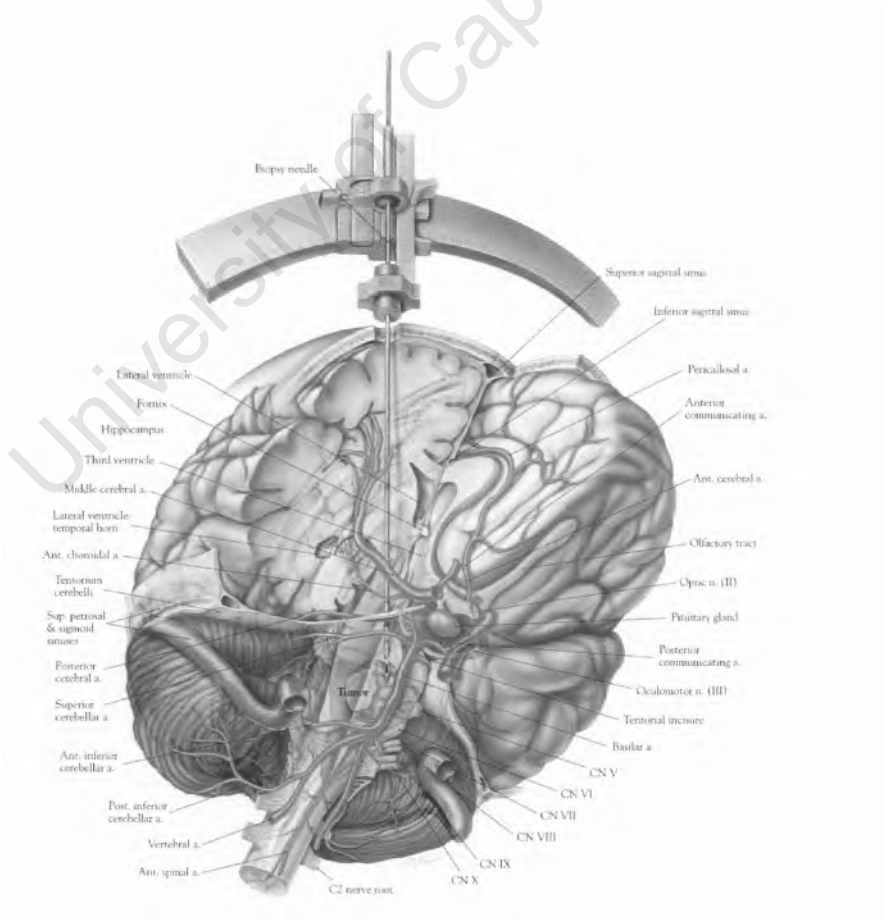


Figure 6.5: The contralateral transfrontal approach to the brainstem, illustrating the trajectory through the brain and the important structures to avoid (from [Amundson] with permission of the American Association of Neurological Surgeons).

The present series included two cases where lesions in the rostra! midbrain were biopsied via transfrontal approach; a firm histological diagnosis was achieved in all cases without any complications. Great care was taken to limit the number of needle passes, leaving the outer cannula of the Sedan needle in place while removing the tissue sample from the inner cannula. The postoperative scans in these cases were particularly significant as they indicated that the biopsy had been taken at the target site, indicating a reassuring degree of accuracy *in vivo.*

Although the halo had been sutured to the scalp for these operations, in cases where an extreme degree of accuracy is required, it is certainly an option to anchor the halo more firmly with a screw in the outer table of the skull.

6.9.2 Pineal

A bewildering array of different neoplasms occurs in the pineal region, and making a firm diagnosis on imaging coupled with assay of tumour markers is seldom possible. Although most lesions in this region require microsurgical resection, with the notable exception of germinomas, which respond very well to radiotherapy, establishing the histology preoperatively facilitates operative planning.

No pineal region tumours were biopsied in this series. Pineal tumours show marked geographical variation and are remarkably uncommon in our practice; no suitable cases were seen during the period over which this study was conducted. Many of these tumours present with hydrocephalus so with the introduction of neuroendoscopy in our service in 2000, this has become an attractive option as it allows definitive treatment by third ventriculostomy as well as biopsy at the same operation.

In planning a stereotactic approach to the pineal region, it is critical to consider the various vascular structures situated above and behind the gland. Another consideration is the diagnostic difficulty posed by the histological heterogeneity of tumours in this location. For these reasons, many neurosurgeons avoided stereotactic biopsy of pineal lesions, but a large retrospective French series of 370 cases from 15 neurosurgical centres reported a very acceptable diagnostic yield of 94%, with the majority of the tumours being germinomas (27%), astrocytomas (26%) and pineocytomas / pineoblastomas (24%) [Regis]. This was achieved with a low rate of complications- mortality was 1.6% and serious morbidity occurred in 0.8%. All five patients who died had haematomas evident on the postoperative scan and three had pineoblastomas, a notoriously vascular tumour. Most of the serious morbidity occurred in patients with firm tumours that had been difficult to biopsy.

Although the surgical approach appeared not to influence the outcome, it seems sensible to approach these tumours from a frontal trajectory, using an entry point 2 cm lateral to the midline and 2-3 cm anterior to the corona! suture [Pell_1994ii]. The Pittsburgh group recommend an even more frontal approach in order to ensure that the internal cerebral veins and roof of the third ventricle are not violated [Dempsey].

610 Results

The major advantage of stereotactic brain biopsy over freehand techniques is a higher rate of diagnosis, coupled with a lower rate of morbidity and mortality; although this technique may represent "the ultimate in terms of efficiency in pathological diagnosis" [Chandrasoma], it also presents a number of challenges at the outset. As one of Chandrasoma's neurosurgical colleagues in Los Angeles has written, "the small quantities of tissue .... may stress a pathology service that is not experienced in processing such material" [Apuzzo 1983].

In evaluating the results of stereotactic biopsy, two separate but related questions should be asked:

- **Diagnostic yield** i.e. was abnormal tissue obtained, allowing a diagnosis to be made?
- **Pathologic accuracy** i.e. is this tissue representative of the lesion as a whole, allowing the most appropriate treatment plan to be implemented?

6.10.1 Diagnostic yield

Given the heterogeneity that exists within tumours such as astrocytomas, coupled with the limited sample size of a stereotactic biopsy, it has been suggested that the term "diagnostic yield" is more helpful than "diagnostic accuracy"; in reviewing 17 of the largest stereotactic biopsy series published, which encompassed a total of 7,741 procedures, an overall diagnostic yield of 91% with a range of 80% to 99% was found. [Hall]

The various factors that may conspire to diminish the accuracy of a stereotactic procedure were considered in chapter 4 and the role of the biopsy instrument has been discussed earlier in this chapter. Selection of an appropriate intracranial target is also central to the success of a stereotactic biopsy; important factors to consider include:

- Regional heterogeneity within a lesion; different regions may need to be targeted in order to ensure representative tissue is obtained
- Non-enhancing lesions may have a lower diagnostic yield
- A specific diagnosis may be more difficult to attain in non-neoplastic lesions

The heterogeneity within a lesion was well demonstrated in a study which defined three zones from which stereotactic biopsies were taken in a series of 29 patients with malignant astrocytomas [Greene]. The highest diagnostic yield (67%) was from the enhancing margin, while the hypodense (and likely necrotic) centre yielded 56%. The lowest yield at 36% was from the hypodense periphery, but notably tumour cells were identified as far as 15mm beyond the enhancing margin. This zone may be characterized by various host reactive phenomena such as inflammation, reactive astrogliosis, neovascularization and oedema.

Although a number of authors suggest that a definitive diagnosis may be more elusive in non-enhancing lesions, Rajshekar's group analysed 29 non-diagnostic biopsies out of their series of 407 cases and found no significant difference between non-enhancing and enhancing lesions [Ranjan].

It appears to be widely agreed that non-neoplastic lesions present a greater challenge than neoplasms, with even the leading centres often finding it difficult to make a specific diagnosis in inflammatory conditions [Revesz].

While careful interpretation of the imaging is arguably the most important factor in locating the lesion, ancillary investigations may be of help. An intraoperative strategy that was proposed some years ago was the use of impedance monitoring to define the margin of a lesion [Gorecki] or the wall of a cyst [Rajshekar 1992]. Directing the biopsy at "hot spots" revealed on metabolic imaging such as MR Spectroscopy and PET scanning may also increase the diagnostic yield in selected cases [Messing-Jünger].

6.10.2 Pathological accuracy

Most series reporting stereotactic biopsies confine their focus to the first question, as the only way to confirm that the neuropathological diagnosis was indeed accurate is to resect the tumour. One of the first authors to address this question was de Divitiis, who reported that a correct diagnosis had been made in 92.2% of cases overall, but found that neuroglial tumours were more challenging, with only 81.5% accurately characterized [de Divitiis].

Chandrasoma and colleagues addressed this question in reporting the pathologic accuracy of CT-guided stereotactic biopsy in 30 patients with mass lesions who subsequently underwent craniotomy and resection, allowing a detailed comparison. The histologic diagnosis led to an appropriate management strategy in 28 (93.3%) of the patients, and was incorrect in 2 (one was a glioblastoma where only necrotic tissue had been obtained and the other a pineal germinoma with a significant granulomatous component, which had been the target for the biopsy).

The key observation however was the fact that correlation between the stereotactic and open biopsy was exact in only 19 (63.3%) cases, which included 11 of 12 non-astrocytic neoplasms and 8 of 13 astrocytic neoplasms; of the 9 cases in whom the correlation was imperfect, 2 glioblastomas had been undergraded as anaplastic astrocytomas, 2 astrocytomas had a significant oligodendroglial component that had been missed and 5 non-neoplastic lesions had simply shown "nonspecific changes" [Chandrasoma]. This series predated widespread use of MRI which may have improved matters somewhat, but nonetheless this remains an important concern.

Although non-neoplastic lesions such as infections, inflammatory conditions and developmental disorders (as in Cases 1 and 14) are particularly challenging for the neuropathologist, glial tumours present an array of challenges too. Great difficulty may be encountered in making the following distinctions, particularly on the intraoperative smear:

- poorly differentiated intrinsic tumour vs. metastasis (Case 12)
- assigning a grade to a glial tumour (Cases 6, 8, 19 and 22)
- well-differentiated astrocytoma vs. glial reaction (Case 50)

Various authors have addressed these challenges [Apuzzo_1987, Revesz, Taratuto]. The finding in this series that 31.6% of astrocytomas were assigned an incorrect grade on smear when compared to the paraffin section was striking. Furthermore, it is clear that the grade assigned to an astrocytoma on the basis of a stereotactic biopsy may need to be reviewed should the patient's clinical course not match this.

6.10.3 The role of the Neuropathologist

Stereotactic biopsy has been referred to as a multidisciplinary procedure that requires a neurosurgeon, a neuroradiologist and a neuropathologist [Aker]. In our experience, many general pathologists express dismay at the small size of a stereotactic biopsy, but this has only been compounded by the advent of neuroendoscopic biopsy, where the samples may be even smaller! As has been stated, a resourceful and interested pathologist is pivotal to the successful application of stereotactic biopsy, particularly when a microforceps is used for sampling [Apuzzo_1987].

The first point of contact with the neuropathologist is typically the intraoperative examination. Although some centres persist in using frozen section [Kim], the small specimens are usually not suitable for this technique and consequently the smear technique has really come into its own. Initially advocated by Cushing and Eisenhardt and refined by Russell in 1937 [Marshall 1973], this technique was more readily accepted in the UK than the USA, until needle biopsy became more widely accepted [Marshall 1974]. With stereotactic biopsy, the surgeon's main concern is not what the exact diagnosis is, but whether tissue sufficiently abnormal to be potentially diagnostic has been obtained, and the smear technique is an excellent way to settle this, quickly.

A smear was performed in 81% of cases in this study, with marked variability in accuracy depending on the diagnosis. All metastases were correctly identified on smear, but this was less reliable for astrocytomas, with 13.7% misdiagnosed; the concomitant difficulties of assigning a grade based on smear have already been mentioned.

It is worth remembering that the smear technique was first introduced by neurosurgeons as a technique to be performed in the Operating Theatre. It is a straightforward matter to gently smear a small specimen between two glass slides and immediately fix the specimen with 50% ether and 50% alcohol (or even spray fixative); this prevents the small specimen from drying, which obliterates any chance of getting a histopathological diagnosis. Should there not be a neuropathologist on site, or even a pathologist with an interest in neuropathology, the slides can then be mailed to a centre where a diagnosis can be made [Maureen Duffield, personal communication]. This may be a very helpful strategy for users of the CTSP working in under-resourced settings.

Sometimes the pathologist, however experienced they may be, simply gets it wrong and it may be helpful to review the histopathology should the patient's clinical course not match their diagnosis.

Case Illustration

Case 42

A 19 year-old man was referred to Groote Schuur Hospital by a senior colleague in Private Practice, having presented with an 18 month history of a left sided thalamic pain syndrome and recent onset of a mild hemiparesis. He had nothing of note in his past medical history or family history; a gaze palsy and mild left hemiparesis were present but systemic examination was unremarkable. MRI scan had been performed and this showed a small rim-enhancing lesion in the right thalamus. As the lesion could also be seen on a contrast enhanced CT scan, a stereotactic biopsy with the CTSP was proposed.

Following attachment of the halo in the right frontal region, a stereotactic planning scan was performed. The biopsy was performed under general anaesthesia; the burr-hole was made 5 cm off the midline and after inserting the biopsy needle, 3 specimens were taken, each time withdrawing the inner cannula and leaving the outer cannula *in situ* in order to avoid repeated passes through the brain.

Histology was interpreted as an epithelial malignancy, possibly a metastatic carcinoma. An extensive work-up for a possible primary tumour was negative.

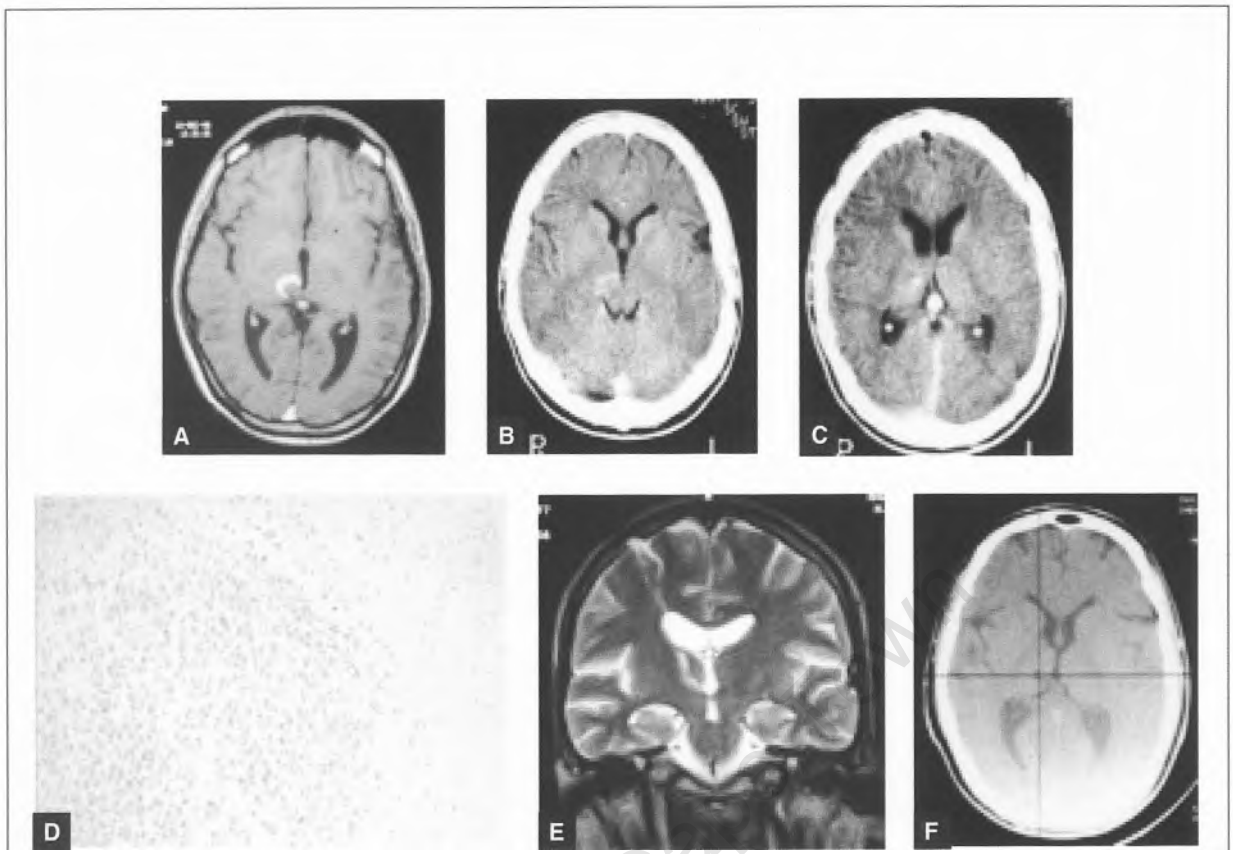


Figure 6.6: Initial gadolinium-enhanced T1 MRI scan (a) showing a rim-enhancing tumour in the right thalamus, also visible on an enhanced axial CT scan (b). CT scan following stereotactic biopsy, demonstrating a new small hyperdensity in the right thalamus, likely a small haematoma at the biopsy site (c). H&E stain showed large cells with prominent nuclei and nucleoli typical of germinoma, adjacent to normal brain, with lymphocytes at the interface; this had been interpreted initially as a metastatic epithelial malignancy (d) and he received proton therapy. Corona! T2 weighted MRI 6 months later shows a hyperintense signal in the right thalamus following proton therapy; the tract of the biopsy needle is also clearly visible (e). In view of symptom recurrence, a repeat stereotactic biopsy was performed (f) and this showed no evidence of malignancy.

Course: The patient was treated with proton therapy and chemotherapy (cisplatinum) with some improvement in his motor deficit and pain syndrome. He experienced worsening of his symptoms 10 months later however and a repeat stereotactic biopsy was performed; this showed no evidence of malignancy and he has remained free of recurrence for the past 12 years.

Comment: The long-term cure achieved with local irradiation (proton therapy) and systemic chemotherapy makes a metastatic carcinoma unlikely and the diagnosis was changed to germinoma on subsequent review of his histology.

6.10.4 What about non-diagnostic biopsies?

As the Toronto group has stated, a failed biopsy poses a real management dilemma [Soo]. Non-diagnostic biopsies may be classified as:

- Negative (Le. missed lesion altogether)
  - Normal brain
  - No tissue
- Inconclusive
  - Necrosis
  - Non-specific inflammation

If the biopsy contains nothing but normal brain, there has clearly been a targeting error. Usually, the biopsy will need to be repeated, although clinical review may occasionally suggest otherwise, as in Case 28 in this series.

Should no tissue be obtained, the technique of biopsy must be reviewed. A related technical problem that has been reported has been the occasional case where the lesion was too firm to penetrate [Muhlbauer]. We encountered this situation in Cases 1 and 14 in this series, where the rather flimsy spiral biopsy needle was unable to penetrate a mineralized lesion.

In a recent series from Brazil, 93% of patients demonstrated histopathological changes on biopsy but a clinical diagnosis was only made in 83.6%; of the inconclusive biopsies, 12 showed normal brain and 14 showed features such as gliosis or necrosis [Teixeira].

It has been pointed out that an inconclusive biopsy may still be helpful [Reigel 1982]. In areas with a high incidence of inflammatory masses such as tuberculosis, it may be very difficult to make a specific diagnosis, but excluding a neoplastic process has definite value. Furthermore, it has been suggested that in some cases it seemed that biopsy had encouraged a response to antituberculous drugs that had previously been ineffective [Rajshekar 1997]!

Before repeating the biopsy, it is important to consider whether obtaining more tissue will necessarily lead to a diagnosis. Having excluded a malignant neoplasm, it may be sufficient to simply follow the patient carefully rather than perform a further biopsy.

Case illustrations

Cases illustrating the challenges encountered in introducing stereotactic biopsy in our centre will be described prior to reviewing the indications, technique and complications.

Case 1

A 6 year old girl presented with a one month history of headache, neck pain and vomiting; no systemic abnormalities or neurological deficit noted. CT scan demonstrated multiple mineralized lesions in the basal ganglia, particularly on the right, with low density change in the adjacent hemisphere.

The patient was transferred to Groote Schuur Hospital for the stereotactic planning CT scan after attachment of the four fiducials to her scalp in the right frontal region. The lesions in the right caudate nucleus were chosen as the target and following satisfactory completion of the imaging and calculations, the patient was transferred back to Red Cross Children's Hospital where the operation was performed under general anaesthesia. The burr hole was made at the pre-determined location and seven specimens taken using the spiral biopsy needle. Histology showed dense calcification but was otherwise considered non-diagnostic.

Course:No specific treatment was offered but her symptoms subsided on follow-up. She remained well and subsequently manifested cutaneous features of Tuberose Sclerosis.

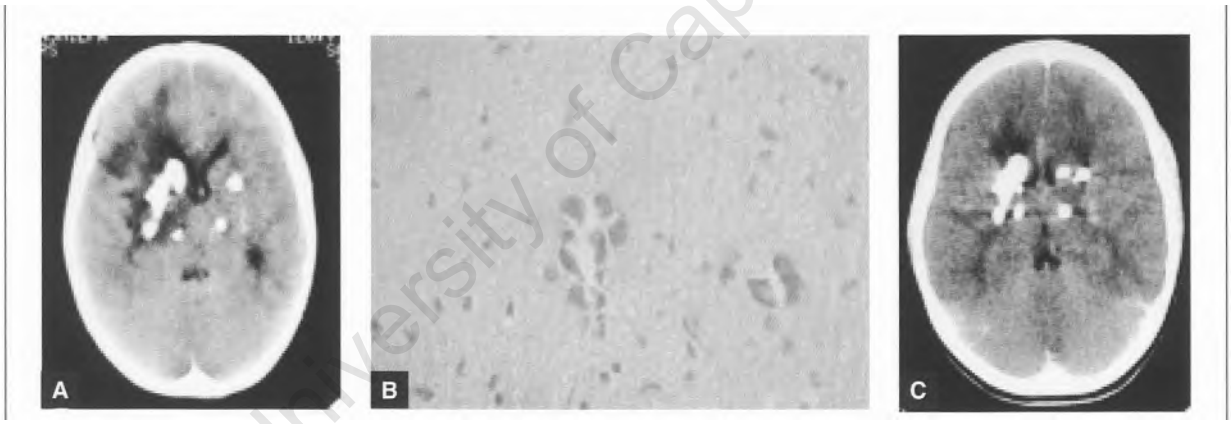


Figure 6.7: Axial CT scan shows mineralized lesions in the basal ganglia bilaterally with low density adjacent to the lesions on the right side (a). Histology showed widespread calcification in the neuropil (b). Follow-up CT scan (five) years later showed resolution of the low density with no progression of the lesions (c).

Final diagnosis:Tuberose Sclerosis, non-neoplastic lesion

Inconclusive biopsy

Problem:Unable to penetrate mineralized lesion

Solution:Firmer biopsy needle required for mineralized lesions.

Case 6

A 51 year old man presented with sudden onset of left sided weakness on a background of drowsiness for 2 months. Examination disclosed left hemiplegia and CT scan showed an inhomogenously enhancing mass in the right thalamus with marked surrounding low density and midline shift. Stereotactic biopsy with the spiral biopsy needle via a right parietal approach yielded four small fragments which on smear were considered *suggestive* of a high grade glioma, but a definitive diagnosis was not possible due to the sample size and extensive necrosis.

Course: In view of the inconclusive histology report, the patient underwent a pterional craniotomy. A total resection was attempted via a transsylvian transinsular approach as the initial frozen section diagnosis was a low grade glioma, but final histology was glioblastoma multiforme. The patient was referred for Radiotherapy but died two months after surgery.

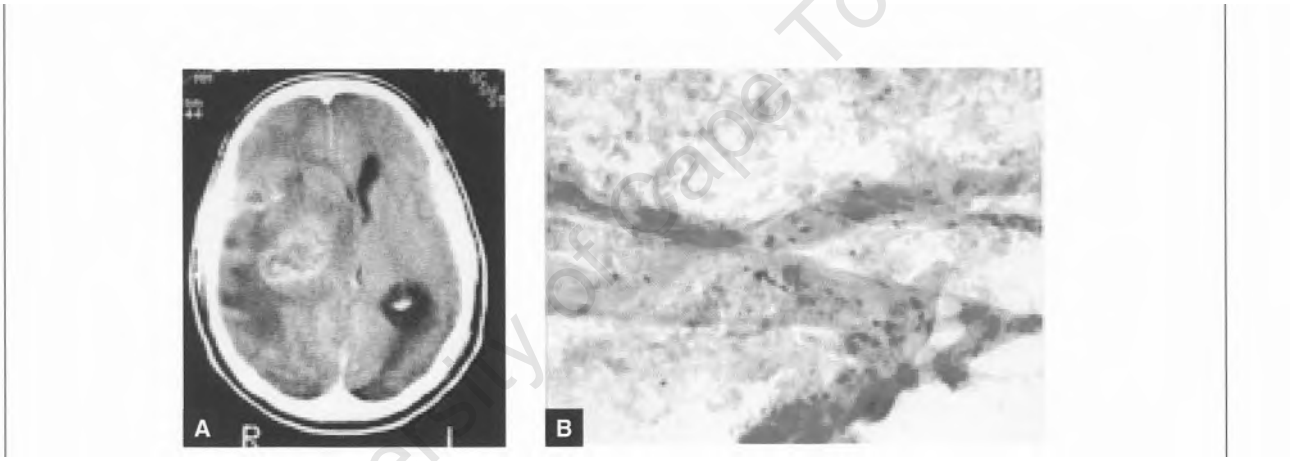


Figure 6.8: Axial CT scan shows the lesion in the basal ganglia (a); the smear preparation shows a tangle of blood vessels with a massively necrotic background (b), making precise identification of the tumour challenging. The specimen was considered insufficient for paraffin sections and the tumour was reported as "suggestive but not diagnostic of a (high grade) glioma".

Comment: Small sample size presents a challenge to the Neuropathologist, particularly early in the introduction of stereotactic techniques

Inconclusive biopsy

Problem: Inadequate specimen due to consistency of necrotic tumour

Solution: Careful selection of biopsy site, avoid biopsying necrotic region

Side-cutting biopsy needle would perhaps have yielded a larger specimen, aiding diagnosis

Case 8

A 53 year old female presented with headache and confusion following a one week history of left leg weakness which had progressed to a hemiparesis. CT scan showed an inhomogenously enhancing lesion in the right basal ganglia.

Stereotactic biopsy via a right frontal burr-hole disclosed inflammation and necrosis, thought to be infective in origin as no neoplasm was identified. The patient was commenced on 4-drug TB therapy as well as intravenous penicillin, chloramphenicol and metronidazole but continued to deteriorate, leading to a second freehand biopsy five days later. This was reported as showing "a large number of vascular channels" but no diagnosis was made. The patient deteriorated markedly three weeks after presentation and died four days after an external ventricular drain was inserted for hydrocephalus. Postmortem examination revealed an extensively necrotic high grade astrocytoma.

Final diagnosis:Glioblastoma multiforme

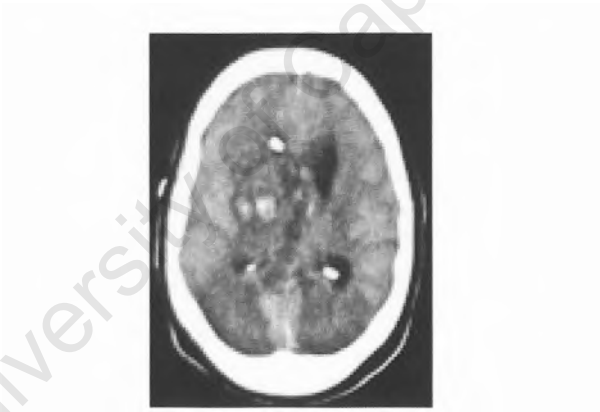


Figure 6.9: CT scan following second freehand needle biopsy and insertion of ventricular drain (initial scans missing)

Problem:Difficulty establishing a diagnosis in the presence of extensive necrosis

Inconclusive biopsy

Solution:Careful selection of biopsy site, avoiding biopsy of necrotic region

Close liaison with Pathologist

Case 12

A 27 year old man presented with clinical features of raised intracranial pressure. CT scan showed a lobulated mass in the left frontal lobe, extending into the corpus callosum and demonstrating peripheral enhancement. Stereotactic biopsy with a spiral biopsy needle yielded disintegrating fragments of tissue which disclosed a *malignant neoplasm of uncertain histogenesis.*

Course:The patient was referred for Radiotherapy but did not tolerate this. He died 3 months later following readmission to Radiotherapy for palliative care and post mortem disclosed a grade IV astrocytoma.

Final diagnosis:Glioblastoma multiforme

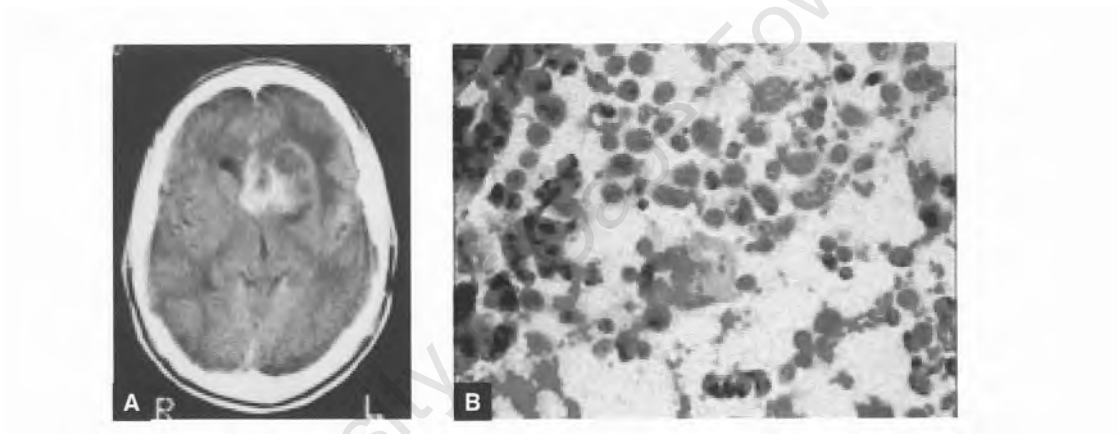


Figure 6.10: Enhancing mass in corpus callosum on CT scan (a); histological review disclosed pleomorphic large cells with prominent nucleoli but no background structure (b), hence this was reported as "a malignant neoplasm of uncertain histogenesis, due to the small amount of material available".

Comment: With a small biopsy specimen, an ambiguous appearance on smear can make it very difficult to distinguish a glioblastoma from a metastatic adenocarcinoma. The imaging appearance was considered to be more in keeping with a glioblastoma of the corpus callosum.
Inconclusive biopsy

Problem:Sample size

Solution:Side-cutting biopsy needle would perhaps have yielded a larger specimen

Case 14

A one month old boy was referred for CT scan for asymptomatic macrocrania; this disclosed a mineralized multiloculated mass in the left thalamus, showing minimal enhancement following administration of intravenous contrast, with a small cyst posterior to the mass.

At three months of age, the patient was anaesthetized and underwent a stereotactic planning CT scan at Red Cross Children's Hospital. The biopsy was performed via a left parietal burr-hole; frozen section of the first specimen showed gliosis and two further biopsies demonstrated haemosiderin laden macrophages and thin-walled proliferating capillaries. No specific diagnosis could be made however.

Course: The patient remained asymptomatic but a follow-up MRI six months later showed the lesion had enlarged. A craniotomy was performed at which time a diagnosis of arteriovenous malformation (AVM) was made on frozen section and the operation was terminated so an angiogram could be obtained. The angiogram showed no evidence of an AVM but was otherwise non-diagnostic; new onset of hydrocephalus necessitated insertion of a left sided ventriculo-peritoneal shunt six months later.

Final diagnosis: Giant capillary cavernous angioma

Figure 6.11: left thalamic lesion (a) showing a lobulated mineralized lesion in the right thalamus. Histology demonstrated abnormal vessels and haemosiderin-laden macrophages (b). Follow-up CT scan 2 years later showed enlargement of both the solid component as well as the adjacent cyst (c).

Problem: Failure to consider a vascular aetiology

Inconclusive biopsy

Solution: Always consider a wide differential diagnosis in atypical lesions.

Case 19

A 21 year old man presented with a 4 month history of headache and mild right hemiparesis having been treated for recent onset seizures at a rural hospital. CT and MRI scans showed a mixed density lesion in the left parieto-temporal region. Stereotactic biopsy with the spiral needle yielded 3 small fragments thought to show features of a grade II astrocytoma.

Course: The patient was referred for Radiotherapy but he became confused and treatment was therefore terminated after 10 Gy. His course was also complicated by a deep vein thrombosis in the calf.

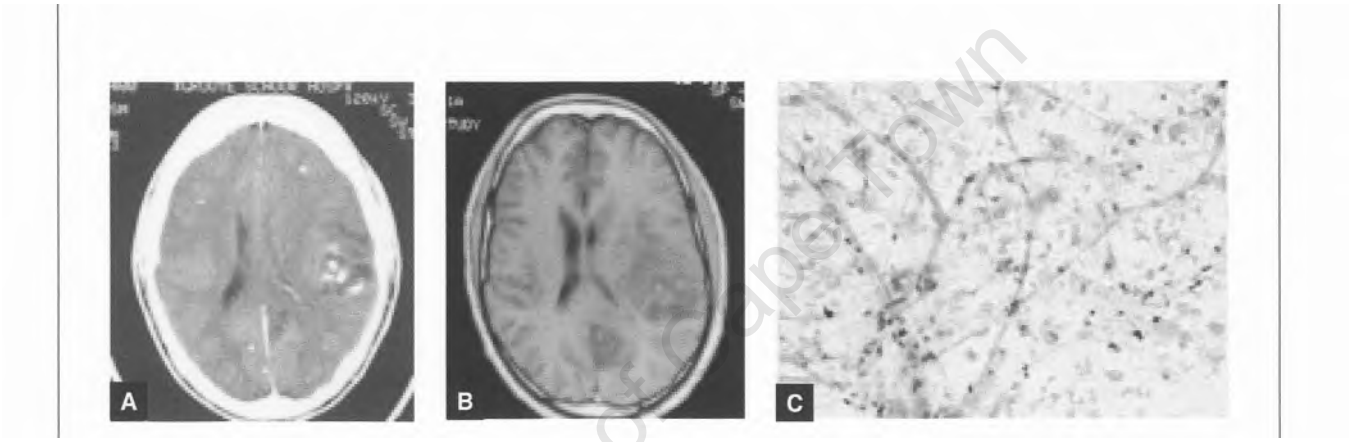


Figure 6.12: Mixed density lesion on CT (a) and MRI (b) scans. Histological review disclosed a cellular tumour with early vascular proliferation (c), making distinction between Grade II and Ill difficult.

Comment: Concern may arise about *under-grading* an astrocytoma following a stereotactic biopsy, but in this case the lack of contrast enhancement was in keeping with a Grade II tumour.

Problem: lower diagnostic yield with non-enhancing lesions

Inconclusive biopsy

Solution: If the diagnosis is pathologically accurate, the patient's clinical course should match the histology.

Case 50

An 11 year old girl with Neurofibromatosis Type 1 was referred from Ophthalmology with a history of progressive visual deterioration over the preceding three years together with a worsening hemiparesis. CT scan showed a hypodense lesion in the posterior left thalamus with peripheral enhancement and marked central enhancement on MRI scan. A stereotactic biopsy was recommended in view of her progressive neurological signs.

At the time of biopsy the needle was felt to enter a firm lesion but the initial histopathology diagnosis was "normal brain". Subsequent review by a Paediatric Neuropathologist noted the presence of a number of Rosenthal bodies, indicative of a Grade I Astrocytoma.

Course:No progression of lesion on initial follow-up, but subsequently lost to Neurosurgical follow-up.

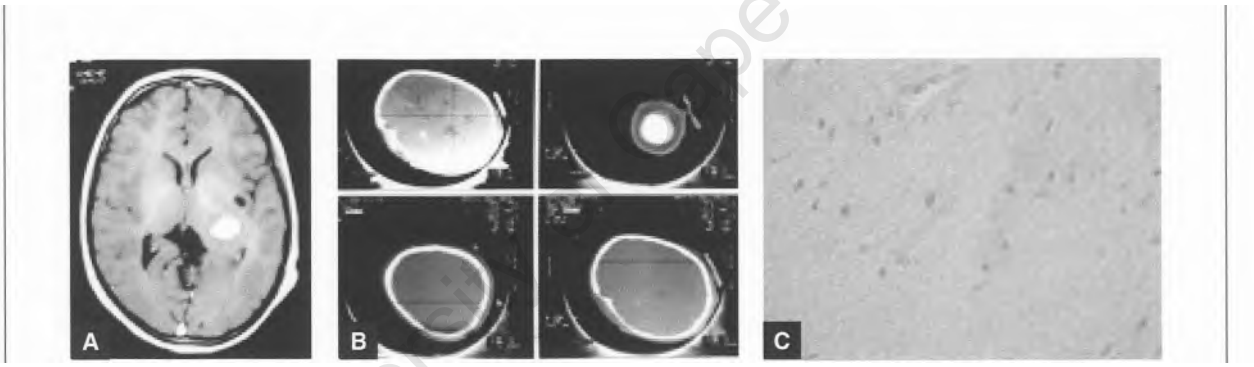


Figure 6.14: Initial MRI showed an avidly enhancing lesion in the posterior left thalamus (a), biopsied via a parietal approach following administration of intravenous contrast for the planning CT (b). Histology revealed a Grade I Astrocytoma with a number of Rosenthal Bodies (c).

Comment: In hindsight, this lesion was typical of a Pilocytic Astrocytoma in the setting of Neurofibromatosis Type 1.

Problem:Difficulty establishing a diagnosis in low grade tumours

Initially negative biopsy

Solution:Involvement of a Neuropathologist in unusual cases

6.11 Complications

The forgoing discussion demonstrates that stereotactic biopsy is an effective and accurate procedure, but it is also important that the surgical objective be achieved at low risk to the patient. Mortality should be very low as this is not a therapeutic procedure. A review of 7,471 biopsies suggests that this is indeed the case- the overall diagnostic yield of 91% was achieved with 3.5% morbidity and 0.7% mortality. [Hall]

Given the developmental nature of this series, and the heterogeneity of the procedures, it is difficult to compare our data, but there was only one death, giving an operative mortality of 0.8% (1 patient/115 procedures) and two patients suffered major morbidity (1.7%).

A recent publication from Pittsburgh sought to establish a benchmark for the complications of frame-based stereotactic surgery through analyzing a 28-year experience encompassing 2,651 cases, most of which were performed in a specially constructed operating room containing a dedicated CT scanner [Lunsford 2008]. Immediate postoperative CT scan detected blood products in only 43 of 1,664 biopsies (2.6%), six of whom required craniotomy for haematoma evacuation. Two patients, early in the series, died as a direct result of their stereotactic surgery, a mortality of 0.075%.

The complications that require particular consideration are:

- Haemorrhage
- Swelling
- Increased or new neurological deficit
- Seizures
- Sepsis
- Implantation
- Systemic, such as DVT

One of the important tasks has been to identify which patients are at particular risk for complications. The Toronto group noted that markedly raised intracranial pressure increased the risk of death due to herniation [Bernstein_ 1994]. Preoperative use of antiplatelet agents, chronic corticosteroid use, biopsy of deep-seated lesions and malignant gliomas and a greater number of biopsy attempts increase the likelihood of complications [Sawin]. A report from Johns Hopkins

confirmed that biopsy of thalamic and basal ganglia lesions carried a higher risk of complications, particularly if more than one needle pass was required, and also found that diabetes with a blood glucose level >200mg/dl had 100% predictive value for biopsy-related morbidity [McGirt].

One study reported a high diagnostic yield taking a median of 14 biopsies per patient with remarkably low complication rate of 1.5% [Fritsch]. Perhaps the number of needle passes is more relevant in this regard than the number of biopsies taken.

6.11.1 Haemorrhage

Haemorrhage is the most feared complication of stereotactic brain biopsy. When it does occur it is usually venous or capillary in origin and arterial bleeding is rare.

Various factors may affect the risk of biopsy-related haemorrhage:

i. **Preoperative factors**

- avoid biopsy of vascular lesions
- coagulopathy or taking aspirin
- uncontrolled hypertension

ii. **Intraoperative factors**

- the site of biopsy, avoiding major surface vessels
- a burr hole enables the neurosurgeon to avoid lacerating a surface vessel
- trajectory selected to avoid crossing more than one pial surface, regions of vessels such as the Sylvian fissure and the supratentorial midline
- technique of biopsy (haptic feedback or "feel")
- avoiding multiple passes

iii. **Postoperative factors**

- blood pressure control

A small fleck of blood on the postoperative scan is common in our experience, and can be quite helpful (as can a small locule of gas) in indicating the site of the biopsy and certainly is no cause for concern but larger haemorrhages may require specific intervention.

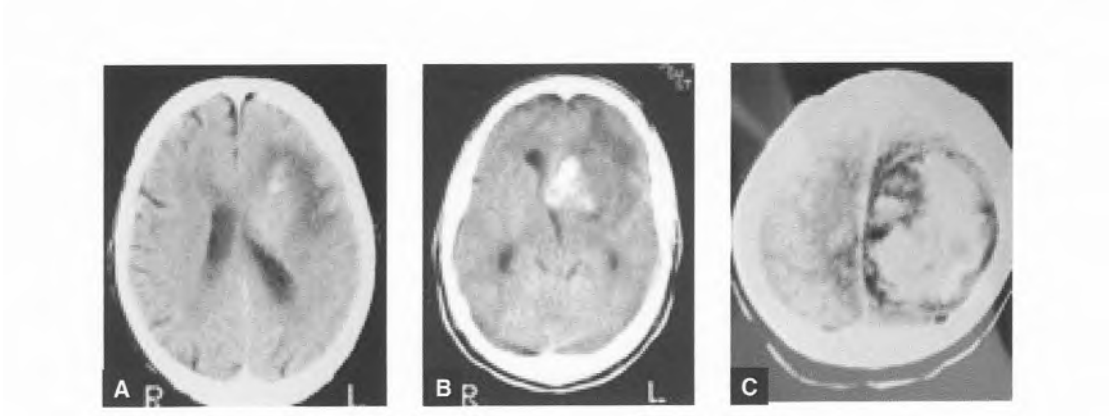


Figure 6.15: Haematomas following stereotactic biopsy. Minor haemorrhage <5mm in diameter (a); moderate haemorrhage which was managed expectantly (b) and large haematoma which required urgent craniotomy for evacuation (c).

As already discussed, many neurosurgeons routinely obtain postoperative CT scans to establish whether there has been intracranial bleeding; in an effort to establish the true incidence of this, Kulkarni and colleagues conducted a prospective study in which 102 consecutive patients who underwent stereotactic biopsy over a two year period underwent a CT scan within 24 hours of surgery [Kulkarni]. Nine patients (8.8%) experienced an early postoperative deficit, of whom threehad no blood evident on their scan and the deficit was attributed to increased tumour oedema. Although six patients who had a deficit also had blood evident on CT scan, a further 56 patients had haemorrhage but no deficit i.e. the haemorrhage was clinically silent. In the majority of cases the haemorrhage was minor; the authors utilized a helpful classification based on maximum diameter which has also been used in this study, with a fairly similar spread (Table 6.1)

Type of haemorrhage	No of patients	
	Kulkarni et al	This series
Intracerebral < 5mm	22.5%	19.1%
Intracerebral 5-10 mm	20.6%	29.8%
Intracerebral 10-30mm	6.9%	4.3%
Intracerebral 30-40 mm	4.9%	2.1%
Subarachnoid	2.9%	
Subdural	1.0%	
Intraventricular	1.0%	
Total	59.8%	57.4%

Table 6.1: Incidence of haemorrhage on postoperative CT scan compared with the series reported by Kulkarni [1998]

While the main recommendation of this publication, namely that routine CT scanning after stereotactic biopsy doesn't add significantly to patient outcome, was indisputable, the incidence figures quoted stimulated a spirited debate and spurred other groups into conducting prospective studies examining this issue. The group from Munich argued that use of a dedicated workstation to plan the surgery and a 1mm biopsy forceps to take the biopsy reduced the risk of bleeding [Kreth 1999] and followed this up with a prospective study where the senior author performed 345 biopsies over a two year period [Kreth 2001]. This study reported an incidence of silent bleeds of 9.6% and haemorrhage-related morbidity of 0.9%.

In the rare event that bleeding is apparent at the time of biopsy, this may be from a surface vessel, which may be readily controlled, or from the biopsy site, which cannot be controlled. It is strongly recommended that the surgeon leave the biopsy needle in place to try to prevent a large intracerebral haematoma forming. Should the bleeding not abate, an external ventricular drainage catheter with large fenestrations may be inserted in order to allow the blood to continue draining and a decision made whether to proceed to craniotomy or obtain an urgent CT scan or angiogram.

6.11.2 Swelling

The one death in this series that appears to be linked to a stereotactic procedure was a 44 year old woman who died five days after biopsy of a large right parietal anaplastic astrocytoma. The patient had been referred following initial management elsewhere; a CT scan reportedly showed a large inhomogenously enhancing tumour with considerable mass effect. Unfortunately the scan could not be traced for review. The patient had been transferred to the Radiotherapy ward three days after an uneventful biopsy but was still receiving dexamethazone. Her level of consciousness deteriorated on postoperative day 5; a CT scan showed no haematoma and she was continued on a high dose of intravenous dexamethazone but continued to deteriorate and died the same day. An autopsy was not performed, but it is highly likely that she died from herniation due to raised intracranial pressure, possibly provoked by the stereotactic biopsy.

Many patients harbouring intracranial lesions which require biopsy will have raised ICP to some degree so this is not in itself a contra-indication to needle biopsy, but great caution is required for the patient with critically raised pressure for whom the smallest volume increment may prove fatal. Of the five patients who died in a series reported from Toronto, all had a glioblastoma multiforme and three died from transtentorial herniation with no evidence of haemorrhage at autopsy [Bernstein]. The authors noted that a small haemorrhage, a slight increase in oedema

or even the volume of the biopsy instrument itself could precipitate herniation in this situation.

6.11.3 Increased neurological deficit

There is no question that patients who already have a focal deficit at the time of biopsy are at increased risk for that to worsen. Another consideration is the site of the biopsy; this has been convincingly shown by a study reported by Cook and Guthrie, comparing the neurological complications of biopsy in eloquent vs non-eloquent areas [Cook] (Table 6.2).

Postoperative clinical status	All patients	Non-eloquent region	Eloquent region
No change	171 (93%)	149 (99%)	22 (68%)
Transient deficit	7 (4%)	2 (1%)	5 (16%)
Permanent deficit	5 (3%)	0	5 (16%)

Table 6.2: The influence of biopsy site in determining whether a patient suffers a postoperative neurological deficit (from [Cook])

6.11.4 Seizures

Anticonvulsants are often commenced in patients presenting with seizures, but stereotactic surgery may itself provoke a seizure. This has been reported in 1-2% of cases in some series [Teixeira] [Blaauw], but given the high incidence of potentially serious drug-induced side-effects we encountered, the use of prophylactic anticonvulsants does not seem justified.

6.11.5 Infection

A single dose of prophylactic antibiotic was usually given to prevent a surgical site infection, as with any other neurosurgical procedure. Of the two surgeons performing the majority of the operations described in this thesis, one gave prophylactic antibiotics routinely while the other did not, which appeared to make no difference in this small series. Shaving the head is not necessary, provided the hair is washed and the surgical site properly cleaned [Blaauw]. The only septic complication was a patient who developed a superficial wound infection 3 days after aspiration of an abscess.

6.11.6 Other

Implantation along the biopsy tract is a rare complication, but it is striking and has been described following biopsy of the following tumours:

- pineoblastoma, in an 18- month old boy, 3 months after biopsy despite having received chemotherapy [Rosenfeld]
- metastasis, in two adults, 6 months and 3 months after biopsy, following treatment with radiosurgery [Karlsson]
- glioblastoma multiforme, 3 months after biopsy [Pierallini, Steinmetz]
- anaplastic astrocytoma, 2 months after biopsy [Kim]

This complication typically presents relatively early after the biopsy and may be reduced by limiting the number of passes of the biopsy needle.

Case reports of various rare complications following stereotactic biopsy include

- traumatic false aneurysm in a 3 year old child following biopsy of a supratentorial astrocytoma, discovered at craniotomy for resection of the tumour; most likely a cortical vessel was injured at the time of the initial biopsy as bleeding occurred at the time of durotomy, although this was easily controlled [Sahrakar]

- pneumocephalus following inadvertent premature removal of the single skin staple following biopsy of an anaplastic astrocytoma in a 79 year old man; this was complicated by acute pulmonary oedema necessitating ventilation [Roth]

Systemic complications such as deep venous thrombosis may also occur, systemic consequences of use of medications such as anticonvulsants and corticosteroids have been mentioned.

6.12 Perspective

Lunsford stated [Lunsford 1993] that there are at least five reasons for failure to obtain a correct histological diagnosis using a stereotactic technique:

- Choosing the wrong patient
- Choosing the wrong technique
- Choosing the wrong imaging tool
- Choosing the wrong surgeon
- Choosing the wrong pathologist

Stereotactic biopsy may appear to carry a long list of potential complications, but it is important to bear in mind the fact that many these procedures are done for lesions that are usually located deep within the brain or in eloquent cortex and often have abnormal vasculature. In that context this really is a remarkably effective and safe procedure.

Performing a biopsy is almost invariably a *diagnostic procedure* which leads to further interventions. Stereotaxis can however be used for *therapeutic* purposes as well; the next chapter will describe an approach to treating a common benign brain tumor, craniopharyngioma, using a stereotactic approach.

Chapter *7*

Stereotactic Chemotherapy

7.1 Craniopharyngioma: the questions

The benign histological appearance of craniopharyngioma belies a malevolent nature, with many patients paying a high price in complications of both the disease and its treatment. This is largely due to the location of the tumour, adjacent to critical neuronal regions, such as the hypothalamus, pituitary stalk and pituitary gland, optic nerves and chiasm, and vascular structures such as the branches of the internal carotid arteries.

The evolution of neurological surgery over the past century is reflected in enormous strides in the management of craniopharyngioma. In reviewing this history, Di Patri observed that Harvey Cushing had coined the term "craniopharyngioma" on the basis that "this admittedly cumbersome term has been employed for want of something more brief to include the kaleidoscopic tumors, solid and cystic, which take origin from epithelial rests ascribable to an imperfect closure of the hypophysis or craniopharyngeal duct." Notably, Cushing himself found this to be "the most forbidding of all intracranial tumors" [Di Patri]

The 1950s brought two major advances in the management of these tumours- the use of corticosteroids and the introduction of the operating microscope. The use of cortisone and adrenocorticotrophin (ACTH) was first reported from Boston Children's Hospital [Ingraham] and this led to a marked improvement in postoperative survival. Not only could potentially lethal postoperative pituitary insufficiency be treated, but surgeons were now able to attempt more radical resections. This was greatly facilitated by the use of the operating microscope which was first used for a neurosurgical operation in 1957 and within a decade, a number of neurosurgeons had reported microsurgical complete resection of craniopharyngiomas [Di Patri].

Among the most ardent exponents of radical resection was Harold Hoffman at the Hospital for Sick Children in Toronto, who in 1977 maintained that total excision could be carried out almost invariably, without mortality or even morbidity [Hoffman]. Another landmark was reached in 1990 when Yasargil reported a series of 144 cases, 93% of whom underwent a total resection [Yasargil]. Radical resection, usually via a pterional or subfrontal craniotomy had become accepted as the standard of care, particularly among experienced surgeons [Sanford]. Ongoing refinement of surgical strategies, particularly the introduction of less invasive approaches such

as transphenoidal resection [Laws 1994] and other applications of endoscope-assisted surgery [Teo], widened the range of options available to the neurosurgeon in striving for this goal.

Another important strategy in managing these tumours has been the use of radiotherapy, delivered in various ways. It has been noted that "one of the longest lasting debates in neurosurgical practice ... (is) ... what is the role of radical surgery, and what is the place of radiotherapy in the treatment of craniopharyngioma?" [Di Patri]. Long-term studies have demonstrated that conventional external beam radiotherapy does indeed improve long term tumour control, especially following subtotal resection, while more sophisticated forms of treatment such as fractionated stereotactic radiotherapy, radiosurgery (either with the linear accelerator (LINAC) or Gamma Knife), proton therapy and intracavitary beta-irradiation have also been extensively investigated [Kalapurakal].

Although craniopharyngioma may be seen in adults, it is more common in paediatric practice, accounting for approximately 6-9% of CNS tumours in children, and this has obvious implications for management in general and the use of radiotherapy in particular. Determining the optimal treatment for craniopharyngioma has therefore been a source of controversy, notwithstanding Fred Epstein's 1992 symposium entitled "Craniopharyngioma- The Answer"!

There is no question that radical surgery has led to a marked reduction in mortality, but long-term morbidity has emerged as a major concern, particularly in children who almost invariably manifest endocrinopathies and severe postsurgical obesity as well as visual deterioration and have a high prevalence of neurocognitive sequelae as well as seizures and motor deficits [Hukin_2007].

In response to these concerns, many neurosurgeons have adopted a more cautious surgical approach, which has been characterized as a pendulum swinging from aggressive to more conservative management [Sainte Rose]. A central tenet of the modern approach is management by an experienced multi-disciplinary team [Hargrave], with the principle goal of treatment being preservation of the patient's quality of life while achieving control of the tumour.

7.2 Intracystic therapy

As craniopharyngiomas arise from epithelial cell rests of Rathke's pouch (the craniopharyngeal duct) or squamous metaplasia, they are of epithelial origin, hence drugs known to be effective against epithelial neoplasms have been utilized in their management. As many craniopharyngiomas, particularly those found in children, have a large cystic component, treatment by instilling such drugs directly into the cyst is an appealing strategy; the agents used most often for this purpose have been B-emitting radionuclides and chemotherapeutic drugs such as bleomycin.

Ayub K Ommaya designed a subcutaneous reservoir attached to a ventricular catheter, which enabled percutaneous access to the ventricles for repeated CSF sampling or direct administration of drugs such as antineoplastic agents and antimicrobials [Ommaya]. This was subsequently manufactured by the Heyer-Schulte Corporation and came to be known as an "Ommaya reservoir". Following a report describing the use of this device for regular decompression of a cystic craniopharyngioma in a patient who had already undergone five craniotomies [Fox], such reservoirs have found application in treating a wide array of neurosurgical conditions are now manufactured in different configurations by various companies.

7.2.1 Radionuclides

The use of intracavitary irradiation in craniopharyngioma was pioneered by the Swedish neurosurgeons Herbert Olivecrona and Lars Leksell, with the latter reporting a case treated by stereotactic puncture of the cyst and injection of phosphorus-32 (32p) in 1952 [Backlund_1994]. Typically, the radiopharmaceutical is stereotactically injected into the cyst as a single dose, without any need for an implanted catheter, which some authorities believe stimulates production of tumour fluid [Lunsford 1994]. This is a relatively simple treatment to administer as it can be accomplished with only local anaesthesia to the scalp.

Building on the work of his predecessors at the Karolinska, Backlund developed an approach to treating craniopharyngioma, the Multimodality Protocol (MMP), in which the choice of microsurgery, intracavitary irradiation, radiotherapy or radiosurgery was guided by a simple classification based on the morphology of the tumour [Backlund_1994].

General morphology	Size/ volume	Type	First choice	Alternative
Predominantly cystic, often one large, solitary cyst	< 5ml	A	MS	IC
	>5 ml	A	IC	
Tumour of reasonable size for safe removal	<10ml	B_{cyst} > 50% cystic	MS	IC (+RS?)
		B_{solid} > 50% solid	MS	RS
Pleomorphic gross anatomy, often many cysts	>10 - <100 ml	C_{cyst} > 50% cystic	IC (+MS?)	(RT?)
		C_{solid} > 50% solid	MS	RT? (or RS?)
Tumour of enormous size, often many cysts	>100 ml	D_{cyst} > 50% cyst	IC (+MS?)	(RT?)
		D_{solid} > 50% solid	MS	RT? (or RS?)

Table 7.1: The Multimodality protocol (MMP): treatment options based on a morphological classification of craniopharyngioma. IC: intracavitary irradiation; MS: microsurgery; RS: radiosurgery; RT: radiotherapy [from Backlund 1994]

This well-reasoned approach advocated microsurgery for small lesions, even if cystic, as well as solid lesions of any size, but emphasized the role of intracystic therapy for the commonly encountered scenario where the cyst volume was greater than 10m1. Although the various forms of external beam radiotherapy were not first-line treatment options, their role was quite clearly recognized.

The ideal situation for intracystic radiotherapy is to utilize a B-emitting agent of high energy that has *limited* tissue penetration together with even dose distribution; those used include ^{32}P, yttrium-90 (^{90}Y), rhenium-186 (^{186}Re), and aurum-198 ("Au). In view of the complex issues pertaining to the manufacture and handling of these isotopes, they are seldom a realistic option in developing countries and will not be considered further in this thesis.

7.2.2 Bleomycin

Bleomycin is an antineoplastic antibiotic secreted by *Streptomyces verticillus,* composed of 2 main glycopeptides, Bleomycin A_2 and B_2 which bind to DNA and causes strand scissions [Umezawa]. It is widely used to treat malignant disease, although most tissues, with the exception of lung and skin, are capable of enzymic degradation of bleomycin. It was first used by Umezawa for the treatment of squamous cell carcinoma in 1966 but CNS application was impeded by poor blood-brain barrier penetration. Various investigators reported using bleomycin for malignant gliomas, delivered via an Ommaya reservoir; craniopharyngioma, given its epithelial nature, was also an attractive target and this was first reported in 1976 by Takeuchi, who noted that production of cyst fluid decreased with "no complication worth mentioning" [Takeuchi].

Takahashi and colleagues injected bleomycin labeled with cobalt-57 into the tumour cyst and reported that the radioactivity decreases rapidly with a half-life of 3 hours; by 24 hours, levels had dropped to around 10% of the initial activity [Takahashi]. These authors reported long-term tumour control and this was followed by other positive results from Milan [Broggi], Lyon [Mottolese 1996] and Sao Paulo [Cavalheiro]. There was consequently general enthusiasm within the Paediatric Neurosurgery community about the potential benefits of this approach [JC Peter, personal communication].

Although the treatment outlined above is often referred to as "stereotactic brachytherapy", this applies specifically to the use of radiopharmaceuticals, hence the term "stereotactic chemotherapy" is used here.

7.3 Case series

As craniopharyngioma is a benign tumour, arrest of further tumour growth coupled with decompression of the cyst to reduce intracranial pressure and optic pathway compromise are important therapeutic goals. Following the initial optimistic reports of tumour control by intracystic bleomycin, delaying the use of radiotherapy in children as well as sparing the hypothalamus and therefore preserving endocrine function, this was considered an option worth pursuing. This was particularly appealing in a developing country context, where preservation of function is rendered even more important given the limited access to endocrine replacement therapy and the difficulty of returning to central hospitals in an emergency. A Brazilian colleague has emphasized the important influence environmental factors such as these have on neurosurgical decision-making in managing children with craniopharyngioma [Zanon_1999].

7.3.1 Methods

All patients presenting to Red Cross Children's Hospital and Groote Schuur Hospital with a largely cystic craniopharyngioma from January 1997 to December 1999 were considered for insertion of an Ommaya reservoir and bleomycin treatment. A protocol for treatment was drawn up by colleagues in Radiotherapy in consultation with Neurosurgery (Figure 7.1).

Initial decision-making:
Predominantly solid tumour: craniotomy and debulking
Predominantly cystic tumour: insertion of Ommaya reservoir into cyst (craniotomy or stereotactic)

Permeability test:
2 weeks after insertion
2m1 fluid withdrawn from reservoir
2m1 Omnipaque injected
Patient position rotated to ensure adequate contrast distribution
CT scan 15 minutes after injection; 5 mm thick slices from one centimeter below tumour to one cm above tumour

Injection of bleomycin:
Schedule: weekly for 6 weeks
Oral analgesia and topical anaesthesia (EMLA) to scalp; mild sedation with oral chloral hydrate as indicated
Repeat CT scan prior to first dose of bleomycin, calculate volume of cyst
Dose 4-6 mg depending on volume of cyst
Mixed with 0.9% saline to a dose of 1U/ ml
Butterfly needle inserted into reservoir
Withdraw cyst fluid equal to volume of bleomycin to be injected + 2m1, stop immediately if significant headache
Inject bleomycin solution and flush reservoir with 2m1 0.9% saline
Fluid to be sent for biochemical analysis (LDH and cholesterol)

Completion of therapy:
Repeat CT scan after 6 weeks

- If significant reduction: follow-up CT in 6 weeks
- If multiloculated, repeat contrast cystogram to establish whether another Ommaya reservoir is required
- If progression of solid component, progress to localized radiotherapy

Figure 7.1: Protocol for the use of bleomycin at Groote Schuur Hospital and Red Cross Children's Hospital

7.3.1.1 Insertion of Ommaya reservoir

The intracranial catheter for the Ommaya reservoir was implanted stereotactically in all cases considered here; one patient who received bleomycin following insertion of an Ommaya reservoir at craniotomy was not included in this analysis. As difficulty was experienced in penetrating the calcified cyst wall with the relatively soft silastic catheter in some cases, even with the wire stylet in place, a *modified Seldinger technique* was devised. This entailed puncture of the cyst with the Backlund spiral biopsy needle; the inner spiral needle was first inserted through the wall of the

cyst using a rotatory action should there be resistance, and then pulled back to make a small perforation though which the could then be inserted with ease. The inner spiral needle was then withdrawn and if fluid typical of a craniopharyngioma was aspirated, a J-tipped vascular guide-wire was passed into the cyst. The outer cannula was then withdrawn and the silicon catheter passed into the cyst along the wire.

After verifying flow from the distal tip, the proximal end of the catheter was attached to a reservoir which was secured to the pericranium in a subgaleal pocket. At the outset of this series the only configuration type of reservoir available for use had a "T" configuration with the inlet port on the undersurface, but a side-inlet reservoir was subsequently obtained.

7.3.1.2 Analysis of response

Details concerning the clinical presentation, management decision-making, treatment given, complications and outcome were prospectively recorded. Hospital records (hospital folders and radiotherapy departmental charts) and neuro-imaging studies were reviewed in preparing this chapter. The response to therapy was classified according to the degree of best response in the standard fashion [Hukin_2005]:

- >90% reduction in volume compared to prior to therapy= Complete Response (CR)
- >50% = Partial response (PR)
- >25% = Minor response (MR)
- Progression defined as at least a 40% increase in tumour size or a clinical deterioration that required intervention

7.3.2 Results of intracystic bleomycin treatment

The results of stereotactic cannulation of craniopharyngiomas were described in Chapter 5.11; this chapter will consider the response to bleomycin in these patients.

Six of the eight children who had an Ommaya reservoir implanted received bleomycin; the first patient (Case 3) was treated with Yttrium and was subsequently lost to follow-up while another 1.5 year old patient experienced such marked improvement with simple decompression of the cyst that a decision was made not to administer the drug (Case 90).

Case	Presentation	Type	Total dose	Response and duration	Bleomycin Complications	Outcome
45	Headache in 15 yo girl, surgery and RT for craniopharyngioma 11 years ago	**A**	34 mg	CR	Temporal lobe low density	Stable for 12 years
48	Rapid visual deterioration and decreased level of consciousness in 5yo boy	**A**	44 mg	MR, stable for 4 years, then required aspiration	Deterioration in visual impairment to blindness on L despite no increase in tumour size, panhypopituitarism	RT after 5 years, stable for 7 years
76	Headache and deteriorating vision in 6yo girl	**B**	24 mg	PR	Diencephalic low density	Died at nine months
80	Headache, deteriorating vision and delayed puberty in 13yo boy	**A**	32 mg	MR, stable for 4 years	Panhypopituitarism	Surgery (transsphenoidal and subfrontal) followed by RT, stable for 5 years
87	Headache and mild right hemiparesis in 14 yo girl, surgery and RT for craniopharyngioma 4 years ago	**C**	20 mg (2 courses of 10mg)	CR	Nil	Died 3 months after 2nd recurrence
95	New onset left hemiparesis after commencing proton therapy	Cyst	25 mg (2 courses of 10mg and 15mg)	CR first course, PR second course, died 3 months later	Low density left frontal lobe after 1st course	Died 10 years later, after 3rd recurrence

Table 7.2: Children receiving intracystic bleomycin. Type: Backlund classification (see Table 7.1). Response according to standard criteria [Hukin_2005].

Of the three adults that were considered for bleomycin (Table 7.3), one experienced such marked improvement in her vision following decompression of the cyst that bleomycin was not administered initially, despite her having had the catheter revised due to a leak on the initial contrast cystogram; she was subsequently lost to follow-up (Case 71). A further patient (Case 73) suffered a major complication with deterioration in her level of consciousness together with a new onset left hemiparesis and CT scan suggested that this was iatrogenic due to inadvertent intracranial penetration of the needle in that there was a new tract haematoma. This patient was also from a rural area and was lost to follow-up after returning home.

A third patient experienced transient drowsiness following her first dose of bleomycin and although she recovered and received six doses of bleomycin, she subsequently manifested a relentless deterioration and died three months after starting treatment (Case 82). No autopsy was performed but her deterioration was ascribed to bleomycin by the treating clinicians.

Case	Presentation	Type	*Total dose*	Response and duration	Bleomycin Complications	Outcome
71	49 yo female; HA and deteriorating vision; from rural area	**A**	**0**	N/A	N/A	Returned to referring hospital, lost to follow-up
73	25 yo female with headache and reduced level of consciousness; from rural area	**A**	25 mg (5 x 5mg)	PR	Confusion while instilling blm, bloodstained fluid aspirated. New L hemiplegia with hyperdensity in frontal lobe (?iatrogenic-needle tract)	Returned to referring hospital, lost to follow-up
82	53 yo female with deteriorating vision, headache, poor memory and personality change over one year	**A**	30 mg (6 x 5mg)	MR	Drowsy one day after first blm instillation, recovered well, then subsequent severe deterioration	Died 3 months after starting bleomycin

Table 7.3: Adults considered for intracystic bleomycin. Type: Backlund classification (see Table 7.1). Response according to standard criteria [Hukin_2005].

Case illustrations

Case 45

This 15 year old girl was first referred from a rural area 11 years previously, having presented with features of raised intracranial pressure. A large suprasellar tumour and marked hydrocephalus were present on CT scan and she underwent bilateral VP shunt insertion, pterional craniotomy and subtotal resection and radiotherapy (total dose 60cGy). She returned with recurrent symptoms of raised intracranial pressure and a large cystic suprasellar mass was evident on CT scan (Figure 7.2)

Course:An Ommaya reservoir was inserted via a right frontal approach and she received 34 mg of bleomycin over a 5 week period. The excellent response (>90% reduction in cyst volume) has been sustained for twelve years.

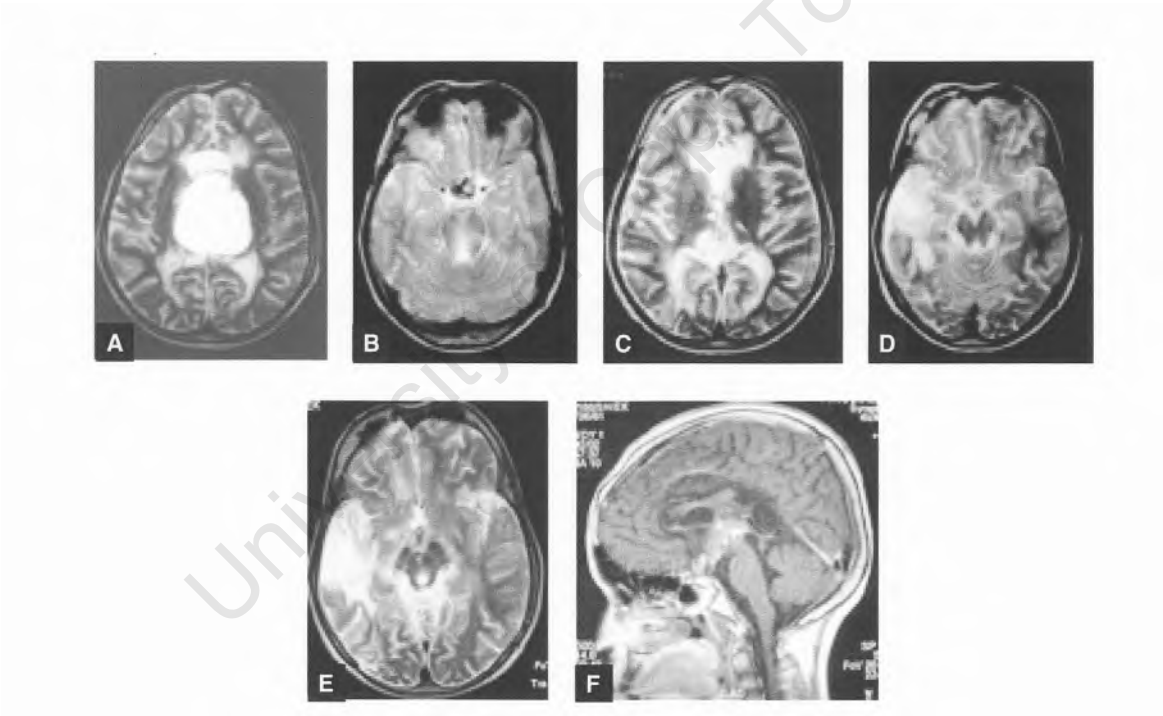


Figure 7.2: Axial T2 MRI at time of tumour recurrence (a) and follow-up image at 6 months demonstrating a CR (b and c); a further follow-up scan at one year showed new hyperintense signal changes in right temporal lobe (d) which had initially been normal in appearance; this was more marked 4 years later (e) although long-term control of the tumour is apparent on the sagittal image with contrast (f).

Case 76

This 6 year old girl had been managed by Ophthalmology for a squint since birth and presented with deteriorating visual acuity; examination disclosed pale chronically swollen discs. CT scan showed hydrocephalus and a cystic mass within the third ventricle with a small suprasellar enhancing mass, typical of craniopharyngioma. Bilateral VP shunts were inserted and within three days of shunt insertion the patient reported improved vision.

As she was considered a good candidate for bleomycin, she underwent stereotactic insertion of an Ommaya reservoir three weeks later. This was accomplished successfully with the blunt-tipped catheter with the stylet in place easily entering the cyst on first pass, following which it was secured to the straight connector of the reservoir. Two weeks later a contrast cystogram demonstrated no leak and the first dose of bleomyin was instilled uneventfully the same day.

Course:Three further doses of 5mg were instilled over the following ten days and she remained clinically well; as the cyst appeared smaller on CT at the time of the fourth instillation, a contrast cystogram was performed at the time of the fifth instillation. Three milliliters of cyst fluid was aspirated following which 4mg bleomycin was injected, mixed with 1 ml of Omnipaque. The patient immediately complained of headache, felt sleepy and then vomited, following which her headache resolved. No leak was evident on the CT scan. Two days later she was found to have mild hyponatremia (131mmo1/1) but she was otherwise well; ten days after instillation of the fifth dose she was drowsy and somnolent and CT scan showed extensive low density in the diencephalon. She was commenced on high doses of intravenous hydrocortisone and ceftriaxone. Her level of arousal fluctuated over the following two weeks but she was eventually fit to go home on a maintenance dose of hydrocortisone.

One month after the event she was readmitted with a reduced level of consciousness and although she had episodes of improvement, she required readmission to the Paediatric Endocrine service on a number of occasions over the following months. Follow up neuroimaging showed atrophy and MR angiography showed diffuse vascular changes.

Overall, her course was one of relentless deterioration with prolonged episodes of hypersomnolence and she died 9 months after the last dose of bleomycin.

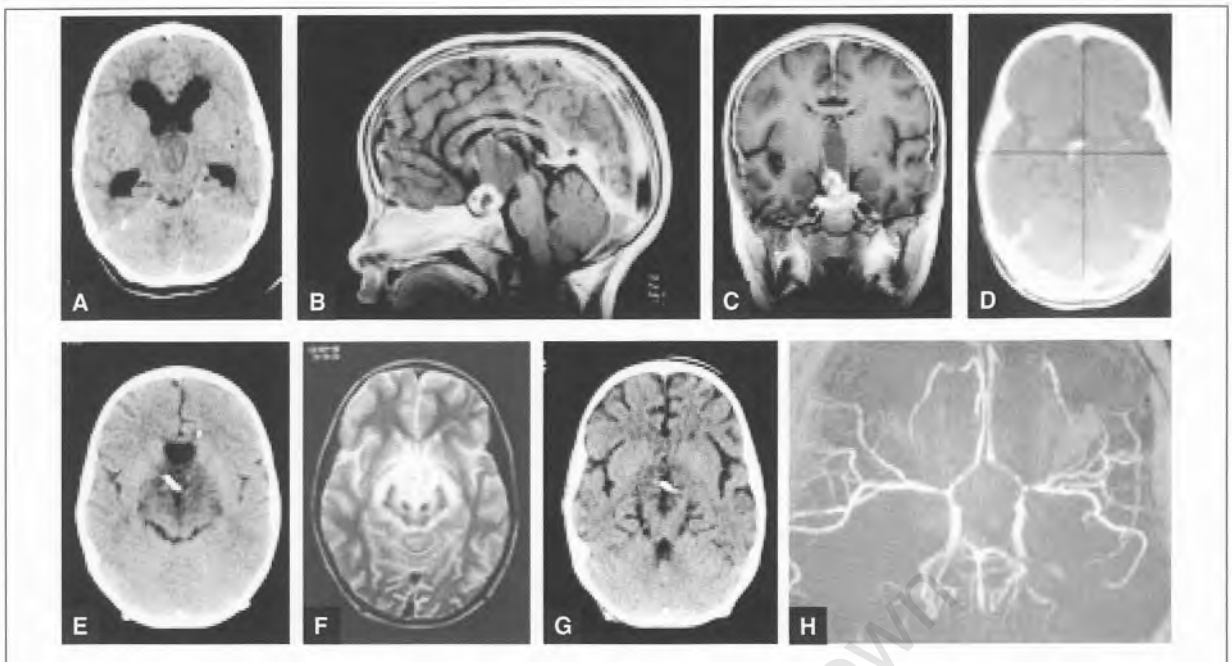


Figure 7.3: Axial CT at presentation (a), sagittal (b) and corona! (c) T1 weighted MRI with gadolinium following shunt insertion, showing the tumour cyst located within the third ventricle. Following the stereotactic planning scan (d), the catheter was implanted successfully in the cyst. Follow-up CT ten days following the last dose of bleomycin showing low density changes in the thalami and midbrain bilaterally (e). Axial T2 MRI 15 days after bleomycin showing extensive hyperintensities in the diencephalon (f) while CT scan 2 months later showed marked cerebral atrophy (g). MR angiogram at 9 months (h) showed diffuse narrowing of both middle cerebral arteries and anterior cerebral arteries bilaterally with a moya-moya blush.

Problem: As a Backlund Type B_{cyst}, perhaps the cyst was too small for bleomycin treatment, although she responded well initially. The apparent absence of leakage may have been falsely reassuring, resulting in her not being treated more aggressively with high dose steroids initially.

7.4 Discussion

The purpose of treating these patients with bleomycin was to control tumour growth while preserving endocrine and neurological function. The technical challenges presented by this strategy will be considered before reviewing the efficacy of bleomycin in this series, together with and the complications of its use.

7.4.1 Technical issues

7.4.1.1 Implantation of the reservoir

Various methods of implantation of the catheter for the Ommaya reservoir have been reported, including craniotomy, stereotaxis and endoscopy. The Canadian Pediatric Brain Tumor Consortium study reported that intracystic bleomycin was utilized in 6 of 17 centres; of the 19 patients selected for this treatment, seven (36.8%) experienced complications related to catheter insertion, with no technique noted to be optimal [Hukin 2007].

Craniotomy is favoured by some as it enables placement of the catheter under direct vision, but even this does not guarantee accurate placement- the first patient in whom we implanted an Ommaya reservoir at the time of craniotomy had a suboptimal position as the tip of the catheter appeared to extrude beyond the wall of the cyst, although no leak was evident on the contrast cystogram. This patient was not included in the present series.

Conversely, some authors have recommended stereotactic placement as a safer option than craniotomy, using a Gordis® tube with only 2 holes at the distal end to avoid leakage, inserted directly with the stylet in place [Mottolese_2001]. This group reported two technical problems early in their series due to misplacement as a result of cyst shrinkage due to tapping first with a Sedan needle.

Ommaya's original design was a T-shaped construct positioned over a burr-hole with the ventricular catheter connecting to an inlet which was perpendicular to the base of the reservoir [Ommaya]. This type of reservoir, manufactured by Codman®, was used at the outset of the study but the design presented a problem as the catheter had to be withdrawn by about 1-2 cm in order to secure the proximal end to inlet of the reservoir, risking inadvertent withdrawal of the tip of the catheter from the intracranial cyst. Later in the series, a reservoir with a side inlet was obtained; this was secured at the burr-hole with an external right-angled sheath and then readily

connected to the inlet of the reservoir which was easily secured in a subgaleal pocket.

The Verona group advocated a protocol they termed the multimodality stereotactic approach (MSA) which enabled insertion of the Ommaya reservoir catheter under visual control following the introduction of an endoscope under stereotactic guidance [Nicolato 2004]. These authors contended that direct visualization facilitated perforation of the cyst wall which they often found to be firm and elastic and, in their experience, this technique reduced the risk of deviation from the stereotactic track, which was clearly a problem in two of the cases reported here (Case 48 and Case 80). A further advantage of the endoscope is the ability to fenestrate septa, converting a multilocular tumour into one that is more readily treated with a single Ommaya reservoir system. In this centre, bleomycin instillation was followed by radiosurgery to the residual solid component, utilizing the Gamma Knife.

A technique for inserting an Ommaya reservoir via "two burr hole technique" using the endoscope has been described from Tokyo [Joki]. Using this approach inevitably requires the catheter to pass through the ventricle which may be more hazardous should there be a leak.

7.4.1.2 Contrast cystogram

This is an essential step in order to ensure there is no leak from reservoir, catheter or cyst prior to instilling bleomycin. In general, 1-2 ml of intravenous contrast is injected into the reservoir and the patient scanned 15-60 minutes later. This procedure is referred to by various other names (permeability test/ water tightness test/ dye test) and has been performed anywhere from 7 days to 5 weeks after insertion of the Ommaya.

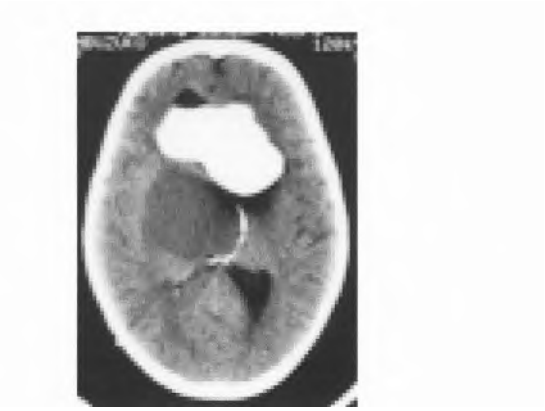


Figure 7.4: Contrast cystogram showing loculation within a multicystic craniopharyngioma (Case 3)

7.4.2 Bleomycin treatment

7.4.2.1 Efficacy of bleomycin

On the whole, these results were not very encouraging. Of the six children treated, three showed a complete response with marked reduction in size of the cyst treated, although two of these patients experienced subsequent cystic recurrences together with growth of the solid component and eventually died, following a decision not to continue pursuing active treatment in view of their generally poor functional state. These three patients had all undergone microsurgical resection and radiotherapy previously. The child whose death was likely due to bleomycin-induced diencephalic injury (Case 76), had shown a prompt response to therapy and may well have had a complete response had therapy not been discontinued in view of this complication. Two children showed a minor response in that the cyst did not shrink to any great extent but there was no progression for four years in both cases.

Both adults who received bleomycin fared poorly, although it is not clear whether this can be ascribed to the drug alone. One patient clearly had an iatrogenic complication in that a new hemiplegia was noted after instillation of bleomycin and CT scan showed a haemorrhagic tract, suggestive of needle penetration, while documentation in the patient who died was insufficient to make a definitive assessment.

The published experience with the use of intracystic bleomycin was reviewed in depth in writing this chapter. The variation in the dosage schedule is quite remarkable, both in terms of the frequency of instillation and the dose administered [Caceres, Hargrave]. Some argue for daily instillation given the half life of 3 hours, but most administer the drug every other day on a Monday / Wednesday / Friday basis; the protocol reported here was at the conservative end of the spectrum in using a weekly dosage schedule. It appears as though daily instillation may increase the risk of severe side-effects [Savas_2000, Jiang].

Most centres administer a dose of 3-5 mg, determining the optimal dose according to the volume of the cyst and often escalating this over time. There may be a correlation between the dose received and the response rate- the Canadian series noted that 4 out of the 5 patients who had a complete response had received a dose of bleomycin that was above the median for the group overall, while 66% of their patients who received a lower dose progressed within one year [Hukin 2007]. Despite this trend, the authors noted that this tumour behaves in a heterogeneous manner in that some cysts will disappear with a small dose of bleomycin and smaller cysts may show little response to a higher dose of the agent; an important caution is the observation that

doses >15mg /week were associated with a higher rate of toxicity in their series.

The variation in efficacy of intracystic bleomycin is perhaps not too surprising given the variation in treatment protocols. The three largest series published reported complete response rate ranging from 29.4% (Canada) [Hukin_2007] through 37.5% (Lyon) [Mottolese 2001] to 50% (Milan) [Broggi 1989]. Of the patients reported in the Canadian multi-centre study, 58.8% required no other treatment and this was the case for 71% of those from Lyon. The combined French/Brazilian series reported a 62% "good outcome" result, although this wasn't defined [Zanon]. In a review published in 2006, the overall results were calculated at CR 23%, PR 51% and MR 26% at a median follow-up of 28 months [Hargrave].

It is striking that the 3 patients (42.9%) who enjoyed an initial complete response, had all received prior radiotherapy. This is not commented on by other authors and from the details provided in the various reports it is not clear whether this was the case in other series.

A theoretical advantage of having an Ommaya reservoir in place is the ability to monitor biological activity through laboratory analysis of the fluid. Takahashi reported that lactate dehydrogenase levels not only fell over the course of treatment, but over time there was also a reversal in the isozyme pattern with a fall in the L5 fraction and a rise in L1. Some authors however have not found this to be reliable [Mottolese 2001].

One of the theoretical concerns about the use of bleomycin is the possibility that this may make later surgery more difficult, but the experience of the Lyon group has been the converse of this, reporting that the tumour was easier to remove as it was firmer with a clear cleavage plane [Mottolese_2005]. The histopathology appears to be unremarkable in tumours resected following a course of bleomycin [Hukin 2007].

Some authors have used bleomycin in combination with radiotherapy, either with intracystic 32p [Jiang] or with radiosurgery [Nicolato 2004]. The complete response observed in the three patients who had undergone radiotherapy some time prior to receiving bleomycin suggests there may be a synergistic effect. It is not clear whether there might be a radiobiological basis for such an effect.

7.4.2.2 Complications of bleomycin

The use of intravenous bleomycin may be complicated by various systemic side-effects such as interstitial pneumonia, pulmonary fibrosis, fever, scleroderma-like skin changes and alopecia [Savas]. It is hardly surprising that this agent may have serious sequelae if it leaks into the brain.

Acute complications

It appears from the literature that minor side-effects such as fever and headache are to be expected following intracystic bleomycin; vomiting occurs infrequently and may have more ominous significance. The major acute side-effects relate to neural injury, the most significant of which is peritumoural oedema in the brain adjacent to the cyst.

The first series published describing the use of intracystic bleomycin in craniopharyngioma commented on the low rate of complications, limited to mild fever in two patients [Takahashi]. A subsequent series reported two serious complications- one patient suffered a middle cerebral artery infarct and another bilateral sensorineural deafness [Broggi 1989]. Another case of deafness was reported from Bologna [Frank] and the Lyon group reported a case of blindness following an incorrect toxic dose [Mottolese 2001]. A case report in 1994 described the onset of hypersomnia, personality changes, memory impairment and thermal dysfunction in an adult shortly after a dose of 5mg had been administered; the patient had commenced on a dose of 0.5mg and tolerated a gradually increasing dose up to that point, with the only adverse effect being a short-lived pyrexia of 38.5° after each dose [Haisa]. Although follow-up imaging showed reduction in the size of the tumour at 9 months, with no accompanying abnormalities in the brain, his hypothalamic dysfunction persisted.

The first death attributed to intracystic bleomycin was reported nine years ago [Savas]; this patient suffered extensive damage to the diencephalon and upper midbrain. CT cystogram had revealed a leak at one month and treatment was therefore deferred and only commenced when she became symptomatic at 5 months. Since then a number of similar cases have been reported (Table 7.5). Four cases with similar imaging findings were reported from Canadian centres. One case from Vancouver [Hader] and three patients out of a series of eight who received a total of 13 courses of intracystic bleomycin at the Hospital for Sick Children in Toronto, developed hyperintense signal change in the brain adjacent to the cyst. This was thought to represent peritumoural vasogenic oedema and was treated with high-dose steroids [Lafay-Cousin]; none of these four patients died however.

In our case as well as those reported by Savas [2000] and Hader [2000], no leak was visible on a CT scan performed immediately after the event. Possible explanations could include diffusion of the drug through the wall of the cyst if it is particularly thin or a reaction within the wall of the cyst which causes a reaction in the adjacent brain or a leak more proximally, directly into the parenchyma of the brain which might not be visible on CT scan [Hader]. The initial signs of this complication may be subtle but progressive and it is worth noting that the Toronto group used high-dose steroids on the basis that this strategy is used to good effect in systemic bleomycin-induced alveolitis and fibrosis [Lafay-Cousin].

Two deaths occurred due to thalamic infarcts in patients three months after treatment with bleomycin and ^{32}P; although they did not have immediate scans, they reasoned that there had been no dislodgement of the catheter as no CSF was ever aspirated. It may be that there was a synergistic effect from ^{32}P being administered simultaneously and interestingly, both these patients had tumours located within the third ventricle [Jiang].

Author	Patient/ Tumour	Surgery/ Dose	Complication	Outcome
Savas 2000 *Ankara*	47 yo female presented with hydrocephalus. Small cyst (10cm^3)	Stereotactic. 56 mg over 8 days	Confusion 5 days after completing course; CT showed diffuse signal change in the diencephalon and mesencephalon	Death 45 days after symptom onset
Hader 2000 *Vancouver*	7 yo female. NS	NS 2mg x15 doses (total 30mg)	Lethagy and panhypopituitarism after completing course. Imaging showed collapse of the catheter-containing cyst but enlargement of a new cyst with peritumoural oedema.	Patient underwent surgery; persistent endocrine deficit although CT changes improved over time
Lafay-Cousin 2007 *Toronto*	5.5 yo female. Predominantly cystic, partially calcified tumour extending into the third ventricle	Endoscopic 3mg x13 doses (total 39 mg)	Persistent headache and vomiting; T2 and FLAIR hyperintensity	Partial L III palsy and mild hemiparesis developed which responded to high dose steroids. Imaging improved but long-term weight gain.
	9 yo male. Large suprasellar tumour with rim calcification	NS. 3mg x11 (total 33mg)	Fatigue and deterioration in memory. Extensive oedema on MRI	Hypothalamic dysfunction. High dose steroids; long-term weight gain but improvement in changes on scan; required surgery for progression.
	12 yo male, developed cystic recurrence frontally and in temporal lobe 4 years after initial diagnosis.	NS. 3mg x 25 (total 75 mg)	Asymptomatic- routine imaging at completion of course. Oedema noted in right frontal lobe and left temporal lobe	No specific treatment given as patient remained asymptomatic. Follow-up imaging showed persistent signal change in frontal lobe.

Table 7.4: Published cases where patients have been found to have peritumoural signal change following intracystic bleomycin. NS: not stated.

Changes in other regions of the brain are more difficult to explain- we had two patients who developed new signal changes in the frontal lobe and temporal lobe, remote from the catheter. A remote cerebellar infarct has also been reported [Park].

While some centres have indeed reported poor results [Frank], it may well be the case that serious bleomycin-related complications have occurred more frequently as many of these may have gone unreported. One author refers to other centres that had discontinued bleomycin due

to complications, citing these as "personal communications" [Hader] while another commented in 2004 that "evidence for mortality related to intracavitary bleomycin treatment is anecdotal" [Nicolato_2004] but it appears as though there are now a number of such anecdotes.

Chronic complications

An occlusive arteriopathy has been found in children with slowly growing basal tumours [Mori] and radiation is known to induce vascular abnormalities such as moya-moya syndrome, cavernous angiomas and stroke [Liu]. A few such cases have been described in patients who received bleomycin and radiation. A patient was reported to have complete occlusion of the clinoidal portion of the internal carotid artery as well as stenosis of the ipsilateral posterior cerebral artery 19 years after treatment of a cystic craniopharyngioma with intracavitary ^{198}Au and bleomycin [Sagoh].

Two patients in the Canadian series developed moya-moya syndrome 4 - 5 years after radiation, one of whom died from a massive middle cerebral artery infarct [Hukin_2007]. A patient who was initially treated with bleomycin and then underwent surgery and radiosurgery developed a moya-moya syndrome manifesting with multiple strokes and frequent transient ischaemic attacks, necessitating bilateral pial synangiosis procedures [Scott, RM]. Six out of a cohort of 20 children treated with radiation therapy were found to have some type of vasculopathy; two had received bleomycin prior to undergoing subtotal resection and radiotherapy. One of these patients developed a moya-moya syndrome with right internal carotid occlusion and the other developed an aneurysm on the right internal carotid along with narrowing of the left internal carotid artery [Liu]. The authors suggest that there may have been an interaction between bleomycin and radiation in these patients. The MR angiogram shown in Figure 7.3 is certainly consistent with a moya-moya syndrome.

7.4.3 New approaches

Systemic chemotherapy has been used with little success in this condition [Hargrave], but the benign and predominantly cystic nature of this tumour makes local chemotherapy much more appealing. Local chemotherapy in the form of carmustine wafers (Gliadel®) applied to residual tumour at the time of surgery has been found to be effective in glial tumours and has also been used in treating a craniopharyngioma [Laws_ 2003].

Interferon alpha (IFN-a) is also effective against squamous carcinoma; the first report of its use in craniopharyngioma achieved modest success by administering the agent subcutaneously

[Jackaki]. A recent series from São Paulo described impressive results after intracystic administration in 21 patients, with 11 (52.4%) achieving a complete response [Ierardi], which thus far has been sustained on long-term follow-up [Cavalheiro, personal communication, 2008].

7.5 Perspective

The essence of modern management of craniopharyngioma is to individualize treatment. Implanting a catheter into the tumour cyst to enable decompression or intracystic therapy is a relatively simple strategy and may be associated with better long-term endocrine function than microsurgical resection. This is particularly relevant in developing countries where access to microsurgery is limited and adequate endocrine replacement therapy precarious.

Although intracystic therapy remains an appealing option in cystic tumours, we now reserve the use of bleomycin for recurrences following microsurgical excision and radiotherapy, on the basis of the experience reported here. A possible synergy between bleomycin and radiotherapy may warrant further investigation.

A number of technical challenges were encountered in implanting the catheter stereotactically but once these were addressed, the Cape Town Stereotactic Pointer was highly effective for this purpose. The majority of patients reported in this series were children; the next chapter will consider the wider uses of the CTSP in paediatric neurosurgery and a range of other settings.

Chapter 8

Other Applications

The major indications for which the CTSP was used were for biopsy of intracranial lesions for histological diagnosis and cannulation of tumour cysts but there were various other applications that are worth noting.

As shunt insertion in children was the first application considered at the outset of this project, as described in Chapter 3.4, meeting the challenges posed by operating on children was an important requirement.

8.1 Paediatric Neurosurgery

While working at Red Cross Children's Hospital as the Paediatric Neurosurgery registrar, the author's interest in stereotactic techniques was stimulated by an editorial in *Archives of Disease in Childhood* written by Thomas and Kitchen [1993], calling for wider utilization of stereotaxis in diagnosing and treating various conditions in children. In view of this paediatric context, it is not surprising that the first presentation of the CTSP in a neurosurgical forum was at the annual meeting of the International Society for Pediatric Neurosurgery in Santiago in 1995 [Peter].

As has been described, the first case in this series was a six year-old girl with lesions in the basal ganglia bilaterally. A total of 27 stereotactic operations were performed in 22 children (Table 8.1); this group therefore accounted for 23.5% of all the procedures. There were 13 girls and 10 boys and their ages ranged from 0.2 months to 16 years with a median age of 6; the most frequent indications were therapeutic in that 11 children underwent insertion of an Ommaya reservoir in a craniopharyngioma (14 operations) and 3 children underwent insertion of a shunt (4 operations). Biopsy of a suspected tumour was performed in 8 children (9 biopsies). As can be seen from Figure 8.1, use of the CTSP in children spanned the entire 6-year period.

Case	Age/ Gender	Procedure	Diagnosis	Comments
1	6 F	Biopsy R basal ganglia	Inconclusive histology	Likely tuberose sclerosis
3*	10 F	Cannulation (Ommaya)	Craniopharyngioma	Treated with yttrium
	11 F	Cannulation (Ommaya)	Craniopharyngioma	Lost to follow-up
14	0.3 M	Biopsy L basal ganglia	Inconclusive histology	Giant capillary cavernous angioma
15	0.2 F	Cannulation (shunt)	Arachnoid cyst	Normal development
21	2.5 F	Cannulation (shunt)	Isolated ventricle	Normal development
39	4 M	Biopsy R midbrain	Pilocytic astrocytoma	Cured following resection
40*	15 F	Biopsy R midbrain	Anaplastic astrocytoma	Recurrence 9 months later
	15 F	Biopsy R inferior frontal	Anaplastic astrocytoma	Died following palliative radiotherapy
45	15 F	Cannulation (Ommaya)	Craniopharyngioma	Bleomycin- good response
48*	5 M	Cannulation (Ommaya)	Craniopharyngioma	Surgeon error- cyst not penetrated
	5 M	Cannulation (Ommaya)	Craniopharyngioma	Bleomycin- partial response
50	11 F	Biopsy L thalamus	Pilocytic astrocytoma	Neurofibromatosis Type 1
55*	14 F	Cannulation (drain)	Hydrocephalus	Infection cleared
	14 F	Cannulation (shunt)	Hydrocephalus	Normal development
60	16 F	Cannulation (Ommaya)	Craniopharyngioma	Cyst collapsed so catheter removed
67	14 M	Biopsy L frontal horn	Anaplastic astrocytoma	Non-diagnostic
76	6 F	Cannulation (Ommaya)	Craniopharyngioma	Bleomycin- fatal complication
78	6F	Cannulation (Ommaya)	Craniopharyngioma	System error- cyst not cannulated
80*	13 M	Cannulation (Ommaya)	Craniopharyngioma	Surgeon error- haemorrhage
	13 M	Cannulation (Ommaya)	Craniopharyngioma	Bleomycin- partial response
86	8 M	Biopsy R basal ganglia	Tuberculosis	Initial response, lost to follow-up
87	14 F	Cannulation (Ommaya)	Craniopharyngioma	Bleomycin- good response initially
88	4 M	Biopsy R thalamus	Pilocytic astrocytoma	Marked developmental delay
95	8 M	Cannulation (Ommaya)	Craniopharyngioma	Bleomycin- good response initially

Table 8.1: Patients 16 years of age or younger who underwent surgery with the CTSP

* Four patients underwent two operations each

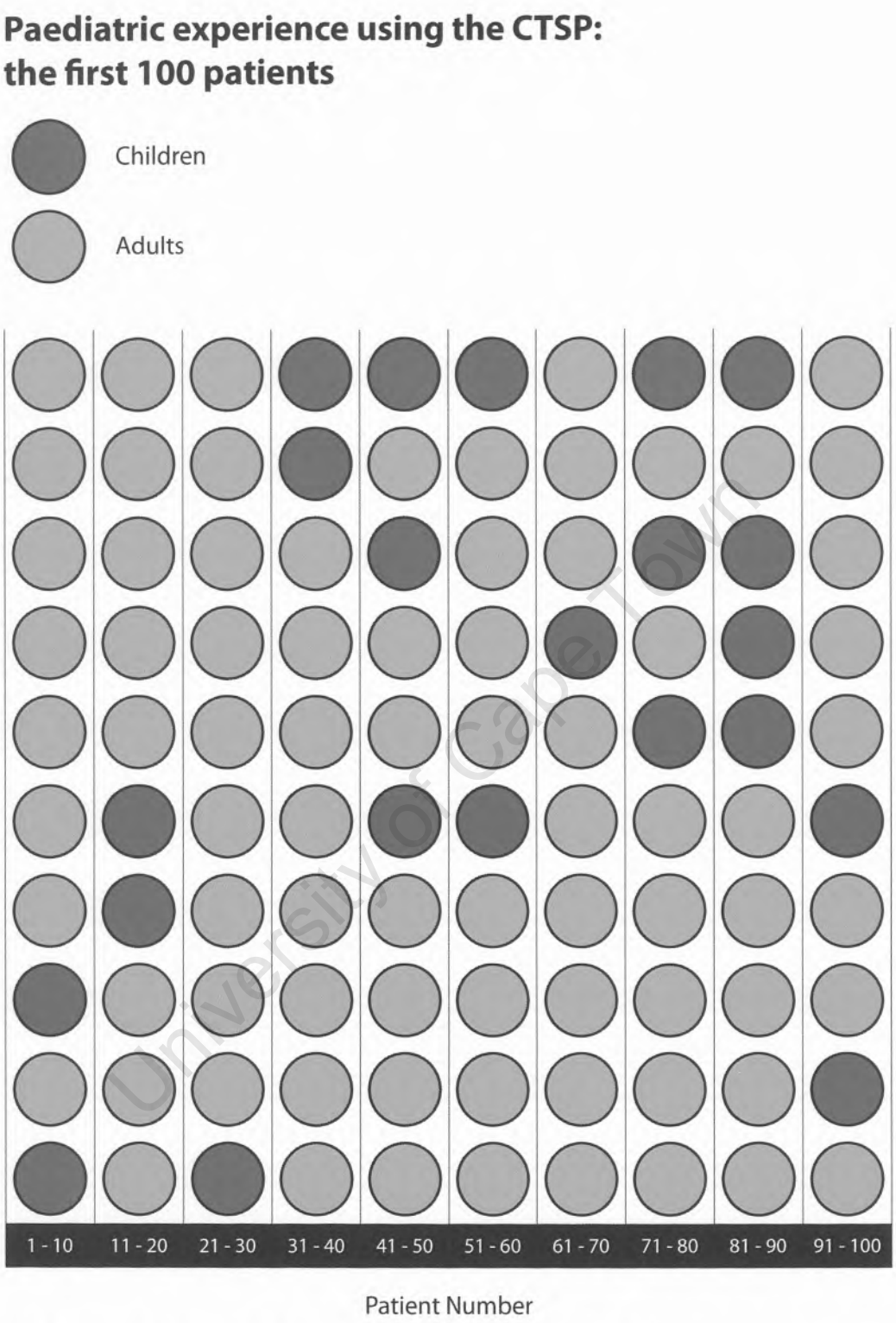


Figure 8.1: Children ≤ 16 years of age undergoing surgery with the CTSP

In the 1980s, recognition of the adverse effects of radiotherapy and chemotherapy on young children turned the tide against the practice of empirically treating lesions found on imaging, without recourse to biopsy. As various centres reported their experience with stereotactic biopsy, children comprised a significant proportion of many large series and a number of reports specifically addressed the issues pertaining to stereotactic neurosurgery in children.

The most frequently cited stereotactic biopsy series utilized the Riechert-Mundinger apparatus to perform 302 stereotactic biopsies, of which 26% were in children under the age of 14 [Ostertag]. A very large series which began with a prototype BRW frame also included children [Apuzzo_1987]; in both of these the youngest child was 18 months of age.

In addition to the publications referred to previously addressing specifically the issue of brainstem tumours in children, a number of more general descriptions of experience with stereotactic surgery in children have been published and these are summarized in Table 8.1. As the paediatric skull has attained 80% of size of an adult by two years of age, size alone is seldom a disincentive to use a stereotactic frame, but one needs to pay particular attention to areas of thinning of the skull due to chronically raised intracranial pressure or previous interventions [Pattisapu].

Some of the challenges that have arisen with the use of conventional stereotactic frames in children include:

- General anaesthesia has been used almost invariably, necessitating particular attention to ensure access to the precarious paediatric airway
- Their smaller head requires longer pins
- Their less rigid skull makes standard pin fixation in the outer table less secure; great care must be taken not to apply too much pressure when drilling the burr hole.

Various inventive strategies to create a firmer construct have been suggested, such as

- Manufacture of a custom-made helmet [Uematsu]
- Application of Plaster of Paris [Thomas 1993, Muzumder]
- Using the hollowed end of rubber tops from Vacutainer blood tubes [Kondziolka 1996].

Author	No and Age range	System	Results	Comments
Broggi 1983 *Milan*	17 cases; 2-16 years	Riechert	Histological diagnosis in all, 7 were candidates for more aggressive therapy	Following CT scan and angiography, metrizamide ventriculography was done to confirm tumour location
'Storrs 1985 *Salt Lake City*	10 cases; 10 mo — 16 years	BRW	Wide range of cases, including stereotaxy-guided excision of an abscess	CT-guided stereotaxic frame provides a level of operative guidance not available with any other technique
Nauta 1986 *Galveston*	9 cases; 9 mo — 16 years	BRW	Repeated successfully in 2 patients following initial non-diagnostic biopsy	Recommended angiography and arterial contrast CT to avoid vascular injury, as well as burr hole to visualize cortical surface
Godano 1987 *Bologna*	34 cases; 1 — 7 years	Riechert	Biopsy successful in 88.2%, no complications	Therapeutic interventions such as draining cysts and ^{125}I implants
Davis 1988 *Rochester MN*	30 cases; 5 mo - 16 years	Kelly	90% diagnosis rate; biopsy followed by craniotomy in 13 of cases	One death following biopsy of a small hypothalamic lesion. Integration of MRI and angiography in planning approach.
'Pattisapu 1989 *Philadelphia and Salt Lake City*	66 cases; 5mo — 18 years	BRW	92% diagnosis rate with 2% complications	Conclusively demonstrated that frame-based stereotactic surgery is safe and efficacious in children
Munari 1989 *Buenos Aires*	134 cases; 2-16 years	Talairach	98.6% diagnosis rate; took 4.01 biopsy specimens/ needle track and 5.39 specimens/ procedure	Sedan Vallicioni needle; high degree of Pathology involvement. 20 cases had unexpected non-tumoral pathology
Black 1993 *Boston*	16 cases; 4-18 years	BRW/ CRW	Biopsy, craniotomy and radiosurgery cases; ^{125}I implants	Used side-biting Nashold needle but found cup forceps better for firmer lesions
'**Walker** 1994 *Salt Lake City*	110; 4mo — 18 years	BRW	96.4% diagnosis rate; comprehensive assessment of use of BRW frame in children	As attempted resection more common in paediatric tumours, needle biopsy required less often than in adults
Herrera 1999 *C6rdoba*	24 cases; 4 mo — 18 years	Riechert	100% diagnosis rate in biopsies; '^{25}I implants	22/24 paediatric cases done under sedation with local anaesthesia
St George 2004 *Birmingham*	15 cases; 4-15 years	Leksell G frame	83% successful biopsies	Difficulty penetrating firm capsule of a pineal tumour

Table 8.2: Published series specifically addressing paediatric issues in stereotactic neurosurgery

Discussion

The CTSP was found to be well suited to children as the halo is light and small. The two youngest children, both under 4 months of age, were operated during the first phase, when fiducials were attached directly to the scalp. The youngest child in whom the halo was used was 1.5 years old, but there is no reason why this couldn't be used in a younger child.

Two decades ago, Rorke argued that the vast majority of paediatric central nervous system tumours require resection, not needle biopsy [Rorke]. There are indeed few indications for stereotactic biopsy in infants and young children and our practice has been to perform definitive surgery rather than simply a stereotactic biopsy, whenever this has been an option. Furthermore, ever-improving instrumentation makes neuroendoscopy an increasingly popular strategy for biopsying lesions such as thalamic gliomas, not least because of the reassurance of directly visualizing the biopsy site.

There are a number of conditions in childhood that are somewhat controversial, such as the approach to a solitary granuloma and the role of biopsy in diffuse brainstem tumours.

Solitary granulomas are typically found in a child presenting with a focal seizure who is otherwise well. Some have advocated stereotactic biopsy of such a "target lesion" in order to distinguish tuberculomas from neurocysticercosis but our approach has been to treat these symptomatically, reserving biopsy for those in whom a tumour features prominently in the differential diagnosis [Domingo]. If a biopsy is performed, it may be very difficult to identify the aetiological agent; Rajshekar reported that tuberculomas could only be definitively diagnosed in 18% of patients with a preoperative CT diagnosis of intracranial tuberculoma who underwent a stereotactic biopsy [Rajshekar 1993].

Following the advent of MRI, it became possible to diagnose *diffuse brainstem gliomas* with confidence in children; although Epstein championed an aggressive surgical approach to focal brainstem tumours, he deplored the use of stereotactic biopsy in diffuse lesions [Epstein]. This position was subsequently supported by a study from the Children's Cancer Study Group, which showed that MRI was highly specific for diagnosing brain stem glioma [Albright]. There may however be a case for biopsy of such lesions in adults [Selvapandian]. Recently there have been a number of reports recommending biopsy sampling in order to direct new therapeutic regimens; use of PET guidance may help to refine the choice of target [Pirotte]. Until clear symptomatic or survival benefit for these unfortunate children is demonstrated, this will remain a controversial

practice.

- An early report from Toronto endorsed the usefulness of frameless stereotaxy in children [Drake], but an ongoing challenge has been the need to immobilize the head during surgery as rigidly fixing the skull in the Mayfield clamp is usually not an option in children under 2-3 years of age. Other groups have addressed this problem [Reavey-Cantwell] and our own experience with electromagnetic tracking with a small adhesive sensor (AxIEM®) has suggested that this is a very promising strategy for navigation during open surgery. For point stereotaxis such as biopsy or insertion of a catheter, our practice is still to use the CTSP, owing to the extreme cost attached to the single-use biopsy kit that is required should one use the navigation system.

8.2 Hydrocephalus

Stereotaxis is seldom required in the modern treatment of hydrocephalus as the ventricles are almost invariably larger than normal and consequently relatively easy to locate "freehand", with the help of external landmarks. Indeed, a skilled neurosurgeon is able to achieve satisfactory catheter placement in over 90% of cases [Pang]. In view of the increased risk of shunt infection due to the additional "fiddle" entailed in using stereotaxis for this purpose, stereotaxis was only used in exceptional cases. It proved helpful in one infant with a quadrigeminal arachnoid cyst (Case 15 as illustrated in this chapter) and two children with abnormal loculated ventricles (Case 21 and 55).

Discussion

One significant advantage of the CTSP over a conventional stereotactic frame is the ease with which the halo can be removed after insertion of the ventricular catheter, facilitating tunneling of the distal catheter.

Stereotaxis has been used to place the proximal catheter of shunt in a variety of different conditions. These include a cystoperitoneal shunt in a prepontine arachnoid cyst [Sweasey], cystoventricular shunts in Sylvian arachnoid cysts [D'Angelo] and a ventriculo-peritoneal shunt in a sequestered fourth ventricle [Montes].

Although the performance of stereotactic third ventriculostomy [Poblete] is now thankfully of historical interest only, stereotactic guidance may be a very helpful adjunct to neuroendoscopy [Hellwig], although very often the ventricles will be sufficiently enlarged for this to be unnecessary.

Case illustration

Case 15

This 2 month female infant was referred to Red Cross Children's Hospital by a General Practitioner following an increase in her head circumference. A quadrigeminal cistern arachnoid cyst had been diagnosed on an antenatal ultrasound; CT scan showed this had enlarged and was causing brainstem compression and there was early ventricular dilatation.

Course: After induction of General Anaesthesia, the fiducials were attached and a stereotactic planning scan performed. Upon returning to the Operating Theatre, the patient was prepared for a shunt with the distal catheter tunneled prior to inserting the proximal catheter into the cyst under stereotactic guidance. Clear fluid with a protein level of 1.59/1 was obtained. Follow-up CT scan confirmed a satisfactory position with decompression of the cyst and at follow-up 16 years later the patient had a normal neurological examination.

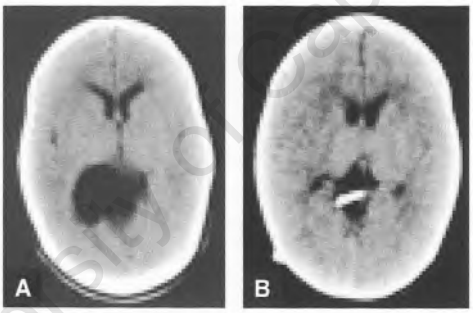


Figure 8.2: Initial axial CT scan (a) demonstrating the cyst located in the quadrigeminal cistern; the postoperative scan confirms placement along the intended stereotactic trajectory (b).

8.3 Brain abscess

Brain abscess carried a high mortality until recent decades, but since the advent of CT scanning, earlier diagnosis has improved the outlook immensely [Moorthy]; improved microbiological techniques and better therapy have also contributed [Shahzadi]. Among the important therapeutic advances has been the use of stereotactic aspiration for abscesses that are small, deep or in critical locations. Although such abscesses can sometimes be successfully managed with intravenous antibiotics alone, failure to respond adequately may mandate drainage in order to isolate an organism.

In this series, 12 adult patients underwent stereotactic drainage of an abscess; 3 patients required two operations each, and one of these went on to require a posterior fossa craniectomy for excision of a separate cerebellar Nocardia abscess. The stereotactic procedure was successful in all but the first patient, in whom brain shrinkage sabotaged the stereotactic procedure; this case has been described in detail in Chapter 5 (Case 2). The only septic complication in the series occurred in a patient who underwent aspiration of an abscess (Case 33). Details of these 12 patients are summarized in Table 8.3.

Case No	Predisposing Factors	Single/ multiple	Location	Size	Organism	Treatment
02	Cyanotic heart disease	Multiple	**R** frontal cortical	20x20x20	No growth	IV clox/ ctx/ metro; no longer a transplant candidate
10	Nil	Single	R centrum	20x20x25	No growth	**IV clox/** ctx/ metro
26	AIDS	Single	R trigone	20x25x20	Amoebiasis	Pyrimethamine and Sulfadiazine
31	Dental	Single	L FP deep WM	20x35x30	Small Gram positive bacilli	IV clox/ ctx/ metro; required re-tap once
32	Previous PTB	Single	L FP subcortical	25x12x15	No growth	4-drug T Rx; IV clox for one week, followed by IV pen and chloramphenicol
33	Previous PTB and empyema	Single	R FP subcortical	20x20x20	Bacteroides	**IV** clox/ ctx/metro; re-tap twice
49	Dental surgery	Single	R deep WM	25x20x20	Strep milleri	**IV** pen/ ctx/ metro
51	Trauma, anterior fossa fracture	Single	R frontal deep WM	10x10x10	Haemophilus influnzae	IV ampicillin/ ctx. Anterior fossa repair one month later
52	Bronchiectasis	Multiple	R frontal deep WM	25x25x20	No growth	IV clox/ ctx/ metro
61*	COAD; referred following 4 aspirations in the private sector	Multiple	R thalamus	20x25x20	Strep faecalis/ Enterocooccus	IV ctx/ metro/ vancomycin. Re-tap 4 days later
	Re-tap		R thalamus	20x25x20	-	Cured
89*	Nil	Multiple	R temporal deep WM	20x15x15	Strep milleri	IV pen/ metro. Re-tap 16 days later
	Different abscess	-	R temporal deep WM	15x15x10	-	Cured
93*	SLE on high-dose steroids, Renal failure	Multiple	R frontal cortical	15x15x20	Nocardia	IV co-trimoxazole/ ctx
	Different abscess		L frontal cortical	15x15x20	-	Craniectomy for excision of cerebellar abscess one month later

Table 8.3: patients undergoing stereotactic drainage of an abscess

* two stereotactic drainage procedures

- clox cloxacillin
- ctx ceftriaxone
- pen penicillin
- metro metronidazole

Case illustration

Case 49

This 32 year-old woman developed severe headache one week after dental surgery; her background history was significant for a liver abscess following uterine perforation. She had no neurological deficit but CT scan disclosed a 2cm diameter ring-enhancing lesion in the inferior left frontal lobe. An extensive medical work-up was negative and she was commenced on intravenous antibiotics (penicillin, chloramphenicol and metronidazole). Follow-up scan 5 days later showed the lesion was slightly larger; her treating neurosurgeon in private practice was reluctant to tap this freehand due to the depth of the lesion and she was referred to our hospital for stereotactic drainage.

At surgery, 5m1 of brown malodorous pus was aspirated and Streptococcus milleri sensitive to penicillin was cultured; she remained on appropriate doses of this agent and subsequently recovered fully.

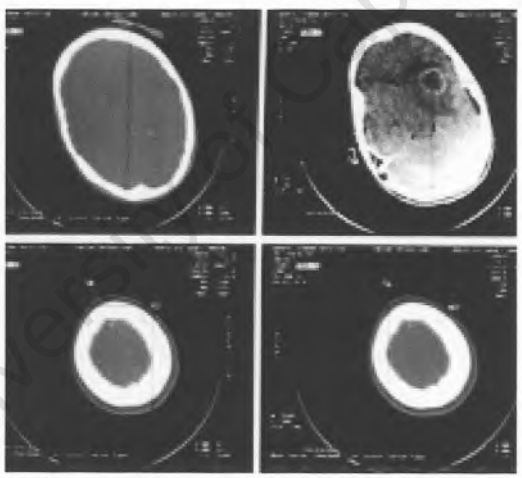


Figure 8.3: Stereotactic CT scan showing a ring-enhancing lesion in the inferior left frontal lobe; 5m1 of pus was aspirated at surgery.

Discussion

Although brain abscesses have diminished in frequency in developed countries, they are still common in developing countries, comprising up to 8% of intracranial masses [Moorthy]. Stereotactic drainage is seldom required for abscesses that present as an emergency and require immediate drainage as these are typically large; for those abscesses that are small or deep, there is usually time to plan stereotactic drainage on the next elective list.

All the case reported here simply underwent needle aspiration without leaving a catheter in situ, but some authors have advocated insertion of a catheter in order to administer antibiotics directly, particularly in patients who are immunosuppressed, have large abscesses or have not responded adequately [Kondziolka_1994]. Aspergillus is an important organism in immunocompromised patients and although our experience has been that these require craniotomy for excision, stereotactic catheter drainage has been reported to be effective [Goodman].

The value of stereotactic drainage is underscored by a review of published literature which found that 82/107 cases (76.6%) had a good outcome [Shahzadi]. As many of these patients will require more than one surgical procedure, there is little question that stereotaxy may reduce the "leucotomy effect" of multiple freehand passes of a brain needle [Moorthy].

Stereotactic approaches may be particularly helpful with an abscess in deep location, such as the case illustrated above; other authors have reported stereotactic aspiration of abscesses located in the brain stem [Rajshekar 1994].

Five patients in this series (41.6%) had multiple abscesses and this also constitutes a good indication for stereotactic drainage [Franzini]. Strategies for decision-making in this context have been proposed [Mamelak] and repeat procedures may be necessary [Chacko], as was the case in 60% of the cases with multiple abscesses reported here.

Steroids are often administered to patients with brain abscesses in order to diminish mass effect from oedema but were only used in 59% of cases reported here; the most likely reason for this is the fact that most of these abscesses were small, ranging in volume from 1.2 — 11 cm^3, with a median volume of 4.2 cm^3.

8.4 Biopsy of intracranial lesions in HIV+ patients

The Human Immunodeficiency Virus pandemic has taken a particularly devastating toll in this country, where the total number of people infected is estimated to be 5.7 million, or 18, 1% of the population, of whom 280,000 are children [UNAIDS]. Data from the first decade of the HIV pandemic indicated that the CNS was affected in nearly one-third of patients with AIDS and 10% of these patients had intracranial mass lesions [Rosenow]. With this background, it is perhaps surprising that only 4% of the patients in this series were referred for biopsy of intracranial lesions in the setting of HIV.

Discussion

Within the first decade of the HIV pandemic, it was established that CNS lymphoma (PCNSL), toxoplasmosis and progressive multifocal leucoencephalopathy (PML) were the most common HIV-related focal brain lesions [Chappel; Levy_1992].

A study from upstate New York reported that HIV-infected patients constituted 11.3% of their stereotactic biopsies; of the 16 patients, 8 had toxoplasmosis and 8 had lymphoma [Plunkett]. The patients with lymphoma had all been treated for toxoplasmosis for 4-6 weeks prior to biopsy.

Making a specific diagnosis in these patients may be challenging for the neuropathologist.
A high rate of non-diagnostic biopsies was reported in HIV [Chappel] and it soon became clear that thorough histopathological evaluation with microbiological backup was required in these cases [Levy_1992, Zimmer]. It is worth emphasizing the fact that the diagnosis in Case 26 was made by the rnicrobiologists on the wet preparation, enabling prompt institution of therapy.

This detailed neuropathological workup does however require considerable expertise and investigations that may not be available in a developing country. In a recent series from Brazil, 15,9% of patients undergoing stereotactic biopsy were known to be HIV-infected; of the 28 patients HIV* patients, toxoplasmosis was diagnosed in 8, lymphoma in 2 and 17 (60,7%) had a diagnosis of "non-specific chronic inflammatory changes". Despite this high rate of non-specific diagnoses, the procedure was considered helpful in that 25% of HIV+ patients had a histopathological diagnosis that differed from the preoperative diagnosis, compared with 14.6% of HIV- patients [Teixeira].

A large study from Verona comparing non-immunocompromised and AIDS patients found no

difference in terms of complications [Nicolato 1997] but one centre reported introducing a coagulopathy protocol in patients with AIDS after experiencing a 12% incidence of intracranial bleeding, 9% of which were fatal [Gildenberg 2000ii]; their complication rate fell to 3% with this measure. Until recently, this report encompassing 243 patients was the largest series of stereotactic biopsies in AIDS and 6.4% of cases had more than one diagnosis.

Survival was dismal prior to the advent of effective therapy, with mean survival 4.4 months after neurological presentation [Levy 1984]. Following the introduction of antiretroviral drugs (ARVs) in 1996, the incidence of PML, PCNSL and toxoplasmosis was halved and the rate of stereotactic biopsies fell steeply [Rosenow]. Of particular interest in this latter study is the finding that no patient who underwent lesion biopsy because of negative toxoplasmosis serology (such as Case 20 above) or atypical neuroimaging findings was diagnosed with toxoplasmosis, emphasizing the importance of both of these investigations in decision-making in this condition.

Case illustrations

Case 20

A 20 year old man with AIDS, tuberculosis and pneumocystis pneumonia developed a left hemiplegia. Initial CT scan showed multiple ring-enhancing lesions in the basal ganglia and the patient was started empirically on pyrimethamine and sulphadiazine, although toxoplasmosis serology was negative. A follow-up CT scan two week later showed a larger lobulated inhomogenously enhancing mass in the right basal ganglia with widespread low density change in the surrounding hemisphere. In view of the failure to respond to a course of toxoplasmosis therapy, a biopsy was indicated. The specimen was reported as showing chronic inflammatory changes in keeping with toxoplasmosis, although no organisms were identified.

Course:The patient was discharged back to the referring hospital for further management but was lost to follow-up.

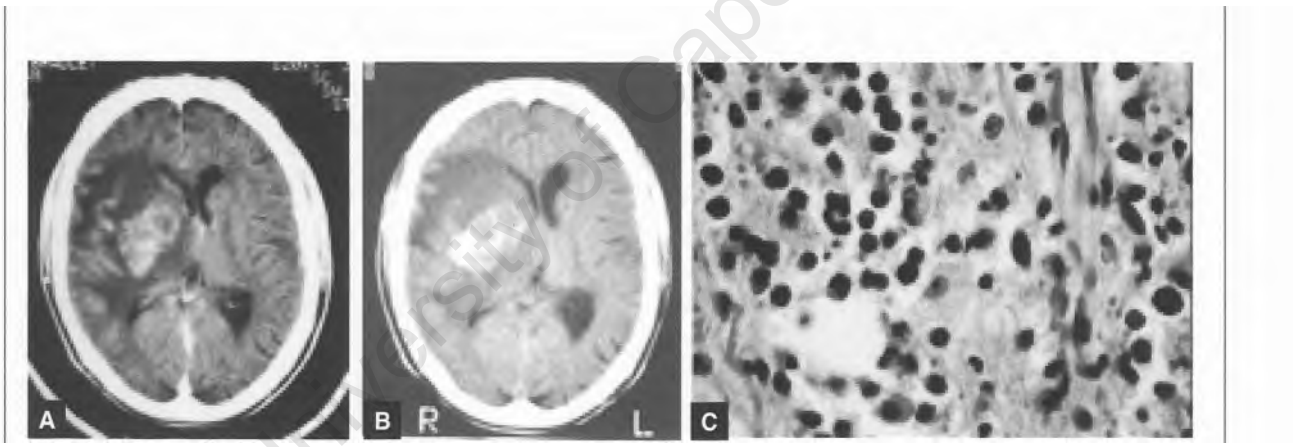


Figure 8.4: CT scan demonstrating a hyperdense mass in the basal ganglia (a), which enhances inhomogenously following intravenous contrast (b). On review of the histology, features of chronic non-specific inflammation were noted (c), rather than the acute vasculitis typically described in Toxoplasmosis. In hindsight, these histological features and the absence of organisms, together with the negative serology, are not consistent with a diagnosis of toxoplasmosis.

Case 26

A 28 year old man with AIDS and a low CD4 count (<10) presented to a referral hospital with headache and a left hemiparesis following the onset of generalized tonic-clonic seizures. Initial CT scan showed a ring-enhancing lesion in the right parietal lobe and the patient was stared empirically on pyrimethamine and sulphadiazine for presumed toxoplasmosis. Follow-up CT scan after two weeks showed progression of the lesion which appeared to be located within the trigone of the lateral ventricle, hence he was referred for a biopsy.

At surgery, adequate biopsy specimens were obtained despite the fact that CSF was also aspirated. Frozen section was reported as showing an inflammatory process and the Microbiologists identified amoebic organisms.

Course:The patient was commenced on appropriate therapy and a follow-up scan one month later showed a satisfactory response.

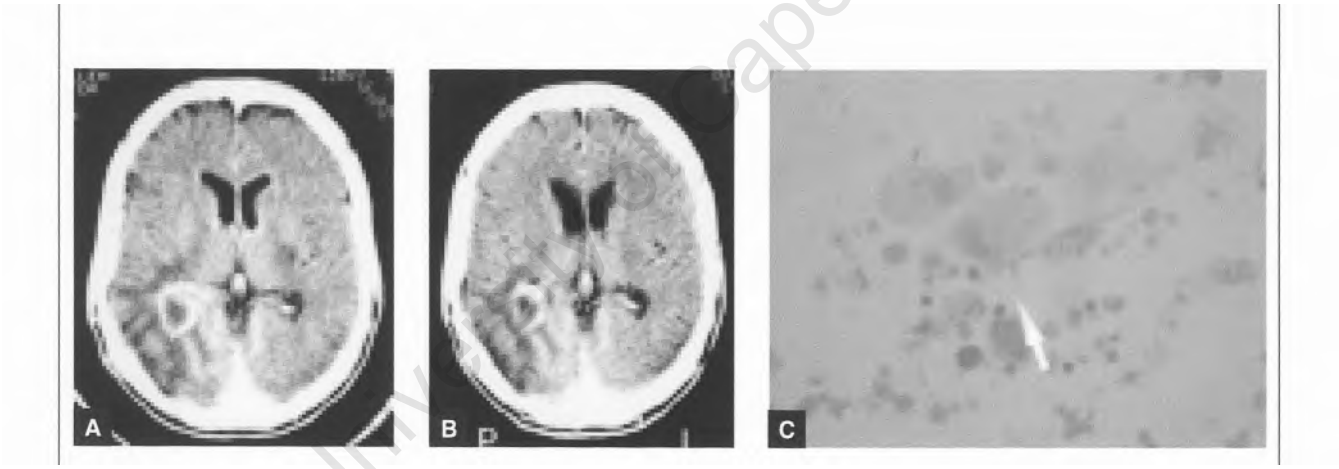


Figure 8.5: Preoperative CT scan showed a ring-enhancing lesion in the right lateral ventricle with marked oedema in the adjacent parieto-occipital lobe (a); postoperative CT scan showed a satisfactory decrease in size of the lesion (b). Definitive histology was reported as showing a necrotizing vasculitis with gitter cells, but on review the latter were thought to be amoebic organisms containing ingested erythrocytes, as shown by the arrow (c).

8.5 Stereotactic craniotomy

One of the more beguiling attractions of modern image-guided surgery is the possibility achieving better outcomes in the radical resection of intrinsic tumours. Having coined the term "stereotactic volumetric resection", Kelly recently suggested that "modern surgical techniques simply allow us to make glioma lumpectomies bigger and safer" [Kelly_2004ii]. However debatable the oncological merits of such an approach for gliomas, being able to accurately locate a small lesion such as a subcortical metastasis, hamartoma or abscess may be helpful.

The evolution of the use of stereotactic guidance at the time of craniotomy has been summarized elsewhere [Ross]. It contended that determining the site and size of the craniotomy preoperatively, based on the optimal trajectory to the lesion, reduces operating time as well as diminishing the risks of wound complications and neurological morbidity [Barnett_1993].

Discussion

For those who do not have a neuronavigation system, a number of simpler techniques for doing this with the aid of a conventional stereotactic frame have been described. Two such approaches were described in a helpful publication from the Cleveland Clinic, one utilizing micro patties and the other a silicone elastomer catheter [Hassenbusch]. The first technique entails placement of 2-3 micro patties at the margins of a tumour, inserting them with the aid of a 4.6mm diameter biopsy needle; after doing so, the stereotactic frame was removed and a conventional craniotomy performed, with the "stereomarkers" providing a degree of resection guidance at the selected margins.

The other technique is somewhat simpler- a catheter is passed into the brain to the predetermined depth adjacent to the tumour and a circumferential suture placed at the level of the cortical surface in order to recognize any migration that may occur. The stereotactic frame is then removed, a craniotomy performed around the burrhole and the catheter followed to locate the tumour. The merits of this strategy have been debated; some consider this a cumbersome approach [Barnett_1993], while in another's experience, once the catheter has been cut off flush with the brain surface, "a subsequent fully sterile and unencumbered microcraniotomy can follow the line of the tube (which moves with the brain) to the target" [Torrens]. This approach was utilized in three cases, one of which was a metastasis (Case 30) and the other two glioblastomas (Cases 37 and 57).

Another option that was explored was the "split" halo, which was designed as a two-piece construct with two thirds of the circumference separated from the remaining third, held firmly together by two screws so that it could be easily dismantled.

This was designed with the intention that the smaller section would be secured with two screws (Figure 8.7), enabling the larger section to be removed and then replaced once a craniotomy had been performed. The tripod could then be mounted on the intact halo and used to locate the intracranial lesion.

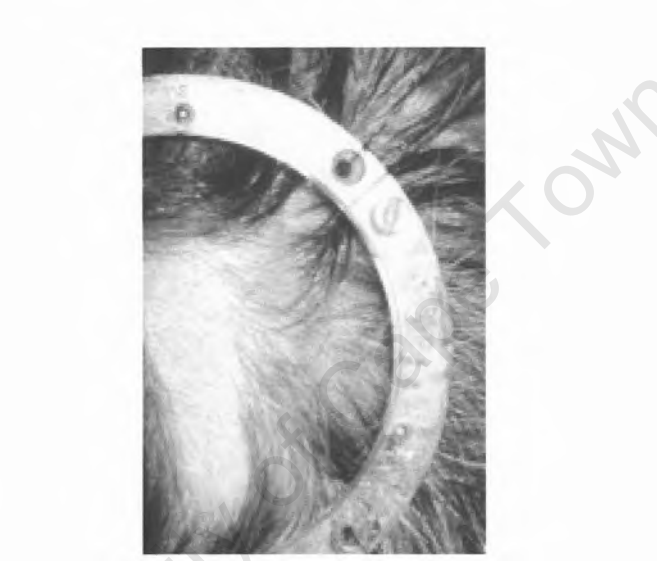


Figure 8.7: The prototype split halo, showing one of the two screws that enabled the halo to be disassembled and reassembled during surgery.

Case illustration

Case 30

This 54 year old man presented with right sided seizures and a hemiparesis, having had a pneumonectomy for stage II adenocarcinoma of the lung 6 months previously. CT scan disclosed a small enhancing lesion in the postcentral gyrus; excision was considered the optimal therapy and stereotactic guidance was used as the lesion was small and located in eloquent cortex.

The CTSP was used to place a burrhole directly over the lesion; the halo was then removed and a small craniotomy performed after re-opening and extending the linear incision made for the burr hole. Postoperatively he experienced no worsening of his neurological deficit and he was referred to Radiotherapy for further management.

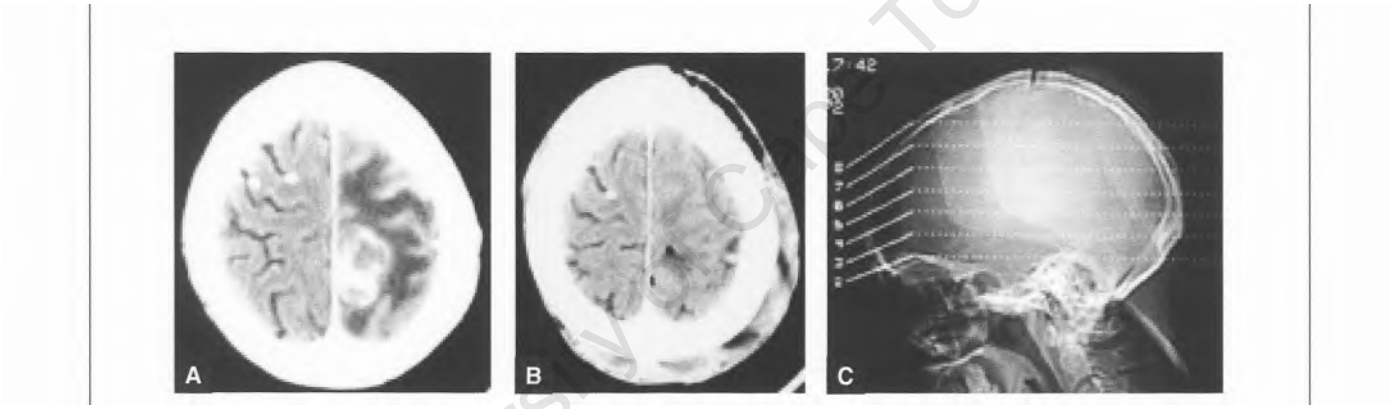


Figure 8.6: Axial CT scan showing the 20x 30 mm enhancing lesion (a) which was removed in its entirety (b) via a small craniotomy (c) which was placed with stereotactic guidance.

Chapter 9

Conclusions

9.1 Performance of the CTSP

This dissertation has described the evolution of a novel stereotactic system from the first clinical application of the concept through a succession of iterations. These successive changes could broadly be divided into four successive phases of refinement which took place over a six year period, encompassing one hundred patients.

Experiments to evaluate the application accuracy had shown a vector accuracy of 1.8 +/- 0.3mm using the setting diagram to set the tripod and 1.9 +/- 0.6mm using the 3D phantom to set the tripod. The present study comprises the clinical counterpart to this laboratory study.

If one excludes the six cases over the period when the incorrect calibration data was used, and one includes as successes the ten cases in which histology was inconclusive or catheters were not implanted but targeting was accurate in retrieving abnormal tissue, the surgical objective was realized in 101/109 cases (92.7%).

Given the fact that six of the eight failures represented errors of surgical judgment that could not be ascribed to the stereotactic system, and each of two system errors resulted in a significant improvement in the system, the Cape Town Stereotactic Pointer demonstrated a satisfactory level of accuracy in clinical application.

This was accomplished with an acceptable rate of complications. Only one death could be attributed to a stereotactic procedure, giving a mortality rate in this series of 0.9%. Two patients experienced major complications (1.7%) and 13 patients experienced minor complications, all of which proved to be transient (11.3%).

A simple protocol for use of the CTSP evolved over the course of this study, making it easier for neurosurgeons from varying backgrounds to introduce stereotaxis into their practice with the help of this system.

9.2 Who is this intended for?

Perhaps the first question to address is, "who should perform stereotactic surgery?" Of course there are large centres where a small number of neurosurgeons can dedicate their time and interest to perfecting their stereotactic techniques and they will doubtless be rewarded with extreme levels of procedural success, but this is a methodology that surely falls within the remit of just about every neurosurgeon. As was pointed out twenty years ago, "stereotaxis can nowadays be performed by any neurosurgeon who can make a burr hole and perform simple arithmetic calculations" [Blaauw].

The author agrees with the view expressed from Cambridge that stereotactic surgery must be practiced by all neurosurgical registrars (residents) in training [Wild], as this is a technique that trainees really should be comfortable with by the time they graduate. Although there is an initial "learning curve", with adequate guidance and supervision this is minimal. One busy neurosurgical service could find no statistical difference in the negative biopsy rate of the most experienced surgeon when compared to seven colleagues who performed fewer biopsies [Ranjan].

Although two neurosurgeons pioneered the development of the CTSP, eight neurosurgeons in all served as the lead surgeon performing operations in this series, with the other six colleagues serving as lead neurosurgeon in 39% of cases.

As the goal was to develop a stereotactic system that would be of help to the general neurosurgeon, it is important to evaluate the advantages and disadvantages of the CTSP in such a setting.

9.3 Advantages of the CTSP

Ergonomic

The halo is easily attached using a strategy that all surgeons are comfortable with, namely insertion of sutures, and this takes no more than 10 minutes. With careful explanation, patients tolerate this procedure well. There is also the option of cranial fixation with one or two screws should this be required and these different options for fixation, either scalp or cranial, constitute a real advantage.

Patient comfort is also enhanced by the fact that the halo is so small and light, with the halo and pointer together weighing just 350 grams. The CTSP compares favourably with conventional

stereotactic frames in this respect as they are usually heavy (weighing around 2 kg) and quite cumbersome and therefore potentially uncomfortable for the patient, with the attendant risk of shifting if incorrectly applied. Furthermore, these systems often require a special device to attach the frame to the scanner table.

Imaging

The patient can be scanned in a comfortable position, although it is ideal for the patient to lie with their head in the same position as for surgery; it is critical to avoid patient movement and adequate explanation helps achieve this. Typically, the scan only takes a few minutes with modern helical scanners. The CTSP is independent of the type of CT scanner and no special headrest or holder is required and basic scanner software is used to determine the co-ordinates.

Protocol for use

Each step of the process is intuitive and therefore easy to understand and little additional training is required for most neurosurgeons, radiographers and nurses.

The Windows-based software is easy to use and can run on any basic personal computer. The user does not have to understand the mathematics and it is a simple mechanical exercise to set the device.

All that is required in order to set the trajectory is to set the co-ordinates on the 3D phantom and then gently apply a depth stop on the surgical instrument. Should the selected trajectory be unsuitable for the position of the burr hole, this is readily adjusted with the burr hole simulator.

Surgery

The small size of the halo means that access to the airway is unrestricted and this particular stereotactic system poses no problems for the anaesthetist. Full sterility during surgery may be ensured by covering the halo with an adhesive drape.

This series has demonstrated that the CTSP is versatile and can be used for various different applications. Most regions of the cortex and subcortical white matter can be reached with ease, as can the basal ganglia and the brainstem via transfrontal approach; the temporal lobe can be accessed if care is taken in positioning the halo.

The halo is easily removed should this be necessary for the next part of the operation, such as shunt insertion or craniotomy. Proceeding to an unexpected urgent craniotomy is straightforward.

Maintenance

The instrumentation is mechanically simple and with the tripod manufactured from stainless steel and the phantom from aluminium, they are durable and readily autoclaved. This is a major factor in developing countries where there is seldom a dedicated instrument technician to care for equipment. The halo cannot be autoclaved but is readily sterilized by gassing or soaking according to local practice.

No routine maintenance is required although damage to the tripod and the phantom, which would render them inaccurate, should be obvious to the user.

Once the calibration data is loaded, this does not need to be altered, unless a different phantom is used.

9.4 Disadvantages of the CTSP

Potential sources of inaccuracy

This is without a doubt the major consideration and the neurosurgeon needs to be absolutely fastidious, but this is true of all stereotactic neurosurgery.

This area has been addressed in Chapter 4, but it bears repeating that the particular steps that require attention include:

- secure attachment of the halo, in an appropriate position
- avoiding scalp movement at the time of scanning and at the time of surgery
- avoiding too great an angle in setting the tripod as this may well magnify inaccuracy
- correct use of the surgical instruments such as the biopsy needle

Neurosurgical insight

Careful planning is fundamental to using this system in that it is not ideal to perform surgery outside the perimeter of the halo. There are a number of ideal entry points, particularly over the frontal and parietal prominences as the halo sits most securely and these are best used; particular care is required should the halo be placed elsewhere, such as in the temporal region.

Limitations

In this series, the CTSP was not used to biopsy lesions in some locations such as the cerebellum and lower brainstem so it is not possible to comment on such applications on the basis of the experience reported here.

Occipital placement is possible, but this may present a minor problem for the anaesthetist should the patient require intubation, which would ideally be performed with the patient turned to the contralateral side.

Multiple trajectories are possible if they can be reached from the same burrhole, but not if bilateral or widely separate in the same hemisphere. In this situation, one could consider attaching two halos. As the halos are manufactured to exactly the same specifications, this is an option.

A burr hole was used for all the cases reported here and it may be difficult to use a twist drill, unless a specific bushing was introduced.

Repeat surgery

The halo is removed after surgery and is therefore not relocatable.

Software problems

Although the program has been designed for ease of use, it is important that the user familiarize himself/ herself thoroughly before doing a clinical case.

It is also critical that the correct calibration data be used, and this should not be altered. It is advisable to check the entered values against the printed values from time to time, and this must be checked in case of an unsuccessful procedure.

9.5 The real cost of innovation

As mentioned in Chapter 3, our rather simplistic goal at the start of this project was "stereotaxis for a thousand rand". This was our first venture into the world of invention and innovation and there were lessons to be learnt.

The initial work on this project was undertaken at the University of Cape Town, by clinicians employed by the Provincial Administration of the Western Cape (PAWC) as well as Biomedical Engineers employed by the University. In terms of the Intellectual Property rules in force at the

time, the South African Medical Research Council (MRC) had ownership of the project as they had provided some of the initial funding to the Biomedical Engineers.

The system was patented (as the "Cape Pointer" with Professor Adams as the Inventor) and the MRC duly appointed an agent, Technifin to take the project to the marketplace. In this company's view, patent protection was required in various countries, including the USA, although the clinicians saw no potential whatsoever for this system to be used in developed countries that already had access to a wide array of sophisticated stereotactic devices.

Technifin licensed the project to a Pretoria-based company, Fibretek, which commenced manufacturing and marketing the device as the "Cape Town Stereotactic Pointer", a name recommended by the clinicians. This company, owned and operated by Mr Peter Mundell, installed the first commercial system in Sunninghill Hospital in August 1997 and within two years had established the system in South Africa. Building on this success at home, they have subsequently sold over sixty CTSP systems in ten countries, with the bulk of the sales being in India, where the local agents, Indelect, have been particularly supportive of the CTSP.

Although innovation is a crucial driver of neurosurgical progress, it brings risks as well as unforeseen costs. Taking an idea "from the drawing board to the bedside" is a process that is unfamiliar to most neurosurgeons [Firlick]. Bringing instrumentation to other neurosurgeons carries substantial costs- not only must the equipment be manufactured to a high standard with the accompanying quality control, but the various other parties who invest time and resources in support require an appropriate return on this. In order to have any impact, money needs to be spent on sales and marketing. Most prospective buyers will want a demonstration in their own hospital and will expect back-up to be readily available following purchase.

Not only is the cost of a piece of equipment a minor component of the ultimate selling price, but the neurosurgical marketplace is small, with approximately 25,000 neurosurgeons worldwide [Kelly 2000ii]. This is compounded by the fact that most of these neurosurgeons practice in North America, Europe and Asia, with only a very small proportion of these neurosurgeons practicing in the developing countries where instruments such as the CTSP have role to play.

The question of the substantial costs incurred through legal protection of the intellectual property is debatable for something that has such a small market and most of these patents have been allowed to lapse.

When the CTSP was first launched commercially in South Africa, it was sold for R10,000 which compared very favorably to the major stereotactic systems which were quoted at over R150,000. None of the South African neurosurgeons who purchased the CTSP had ever used stereotaxis before and all required hands-on training, supplemented by brochures, videos and telephonic support. Many of these neurosurgeons have subsequently gone on to acquire navigation systems as these have become more widely available, and this is an obvious progression.

9.6 Global impact

Over the years, most of the published literature on the use of stereotaxis has emanated from developed countries, with the exception of India which has a long tradition of stereotactic neurosurgery [Ramamurthi_2000]. Recently however, stereotactic articles have been published from developing countries such as Brazil [Ferreira] and Turkey [Calisaneller].

At the time this project began, no stereotactic neurosurgery was being performed in Cape Town and this was also the case in virtually all African countries. The first country outside of South Africa to acquire a CTSP was Kenya, where Mr MM Qureshi started to use the system in Nairobi. He subsequently presented his experience at the Asian Australasian Congress of Neurological Surgery in 1999 and has since served as an enthusiastic reference. Elsewhere in Africa, systems have subsequently been installed in Nigeria, Botswana, Uganda, Libya and Angola.

The country where there has been the greatest impact is without doubt India. Shortly after the production system became available, the author was invited to present at the inaugural meeting of the Indian Society for Stereotactic and Functional Neurosurgery ("Stereocon") held in New Delhi, India in December 1997. There was immediate interest in the CTSP and the first system was sold in 1998. An enthusiastic local agent, Indelect, was subsequently appointed and a hands-on workshop was held at the 8th Stereocon in Bangalore in 2004. To date, 38 CTSP systems have been sold in India (Figure 9.1), one has been sold in Sri Lanka and enquiries have emanated recently from Iran [PJ Mundell, personal communication].

Interest was expressed by colleagues in Colombia and a similar hands-on workshop was held in November 2005 at the Colombian Congress of Neurosurgery in Cartagena des Indias and one system has been sold in South America sofar. The CTSP is currently in use in ten countries around the world (Figure 9.1); to date, over sixty systems have been sold in a total of nine countries and one system has been donated to a mission hospital in Uganda [PJ Mundell, personal communication].

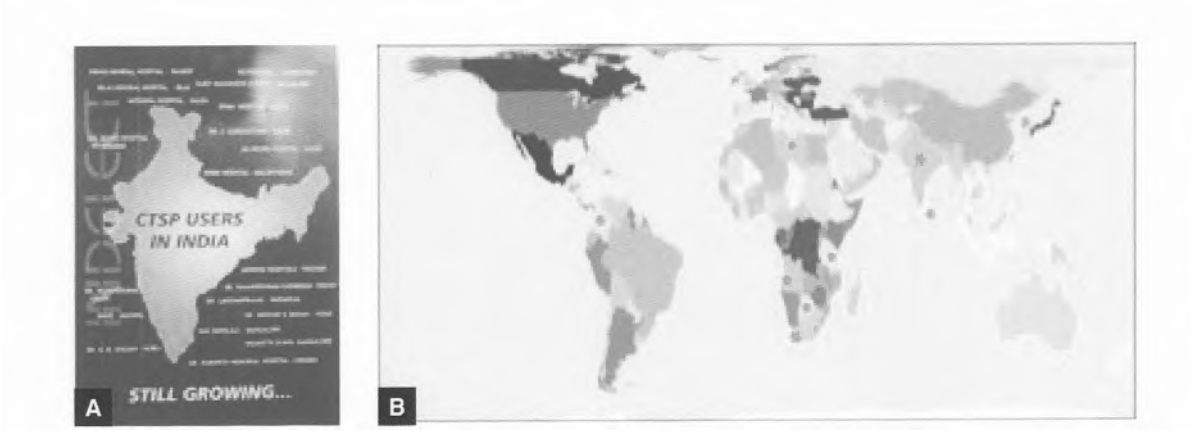


Figure 9.1: Global reach of the CTSP. The CTSP has proven to be popular in India, with a total of 37 systems having been sold there (a); at present, the CTSP is in use in 10 countries around the world, namely, South Africa, Kenya, Nigeria, Botswana, Uganda, Angola, Libya, India, Sri Lanka, Colombia (b).

As was the case in South Africa, a great deal of support and training has been required. This has taken the form of repeated visits to a host of hospitals by Fibretek and Indelect, production of training brochures and videos and conducting hands-on workshops (Figure 9.2)

Figure 9.2: The author conducting a Hands-on Workshop with assistance from Mr Ganapathy Padmanabhan at the 8th Stereocon in Bangalore.

9.7 Future developments

No stereotactic system is immutable and it has been noted that in this field, "the principles of survival (are) simplicity of use and utility of function" [Bakay]. Following the initial commercialization of the CTSP, there has been a continuous process of product development which has been gratifying to witness. This is testament to the versatility of the system, the ingenuity of the users and the commitment of the manufacturer and his distributors. Novel applications of the CTSP have been introduced by other users, such as:

i. Posterior fossa approach

Dr Manjunath Prasad of Hosmat Hospital, Bangalore, was able to perform a transcerebellar approach to biopsy a lesion in the cerebellar hemisphere, with the halo mounted in a suboccipital position.

ii. Haematoma aspirator

It has not been our practice to aspirate deep intracerebral haematomas, but this is the case at some centres and various neurosurgeons requested a haematoma aspirator be supplied. An effective instrument for this purpose, based on the Archimedes water-screw principle, had been devised by Backlund [Backlund_1978] and modified by Higgins and Nashold, who added an irrigation port with a distal aperture near the instrument's tip [Coffey] and such a device is now available with the CTSP.

iii. Functional adaptor

Our intention in developing this system was to facilitate access to point stereotaxis for morphological applications, such as tumour biopsy, aspiration of abscesses and catheter implantation. Although we did not advocate its use for functional applications, some users have suggested that the CTSP could be used to guide implantation of a device such as a Bennett sphere. Such devices have been used for electrophysiological determination of the optimal site for creating a lesion [Eljamel].

iv. MRI halo

As the CTSP halo is such a simple construct with just three fiducials, manufacture of an MRI-compatible halo was a straightforward undertaking and the first MRI halo was manufactured with the ball bearings replaced by 2 mm3 drops of evening primrose oil. A test phantom was constructed, similar to that described in Chapter 4.5, except the evening primrose oil was used for the targets in place of ball bearings. The targets were localized to an accuracy of 2.5 +1- 0.5 mm in a preliminary accuracy study, but the halo was not used clinically by our group due to a concern that potential distortion due to chemical shifts could not be determined as both the fiducials and the targets comprised evening primrose oil [Meintjes].

An MRI halo has subsequently been manufactured using dilute copper sulphate for the fiducials and a phantom study to evaluate this is feasible [B Spottiwoode, personal communication].

9.8 Perspective

In 1958, Austin and Lee wrote "... it seemed to us that the ideal type of stereotaxic instrument should be based on simplicity and ease of handling in order not to become confused with the idea that the more elaborate the instrument the more accurate the subsequent injection or coagulation" [Austin]. A similar philosophy guided the development of the CTSP.

Having developed a system that was easy to use and well tolerated by patients, and also had an acceptable degree of accuracy in the laboratory matched by satisfactory clinical performance, it was important to the developers that this be available to as wide a group of colleagues as possible. This required the system to be sold at a realistic price in order to be cost-effective, but this was not something over which the developers had any direct control. The fact that over sixty of these systems have now been sold, many on the basis of recommendations by current users, suggests that a need has been met.

The late Dr A Sehgal, one of the pioneers of Indian Neurosurgery and the man who convened the inaugural meeting of the Indian Society for Stereotactic and Functional Neurosurgery (IndSSFN), told this author that he believed that the CTSP had played an important role in the growth of IndSSFN through widening access to stereotaxis in his country [Personal communication, Marrakech, 2005].

Simple technology such as this is therefore able to play an important role in building neurosurgical infrastructure and expertise. Doctors progress and patients benefit, and this surely this is a hallmark of technology that is appropriate.

Appendix I

No	A/S	Presentation	Imaging	Location	size & volume	Operation	Diagnosis	Postop scan	Hx	Complications	Assessment
1	6 F	headache and vomiting for one month	bilateral calcific nodules in the basal	R and L basal ganglia	25x15x30 5.9 ml	Biopsy R frontal	Inconclusive (neuropil calcifiication)	Y: d1	No	NIL	Partial success; inconclusive histology
2	46 F	sudden headache	ring-enhancing lesion	R frontal cortical	20x20x20 4.2 ml	Aspiration R frontal	Abscess	Y: d1	N/A	NIL	Failed; surgeon error (brain shift)
3_1	10 F	diencephalic syndrome; headache, vomiting and L hemiparesis for three years	calcified cyst wall	suprasellar	45x60x50 70.7 ml	Cannulation L frontal	Craniopharyngioma	Y: d1	N/A	bradycardia and hypothermia	Successful
3_2	11 F	2nd procedure- new loculated tumour cyst	calcified cyst wall	suprasellar	50x50x50 65.5 ml	Cannulation R frontal	Craniopharyngioma	Y: d1	N/A	NIL	Successful
4	46 M	R focal seizure and hemiparesis	subcortical ring-enhancing mass	L parietal subcortical	40x30x30 18.9 ml	Biopsy L parietal	Adenocarcinoma	Y: d3	Y: <5 mm	NIL	Successful
5	25 F	AIDS; blind with headache and L hemiparesis	avidly enhancing mass	R thalamus	20x20x20 4.2 ml	Biopsy R parietal	No diagnosis made	Y: d7	N/A	NIL	Failed; system error
6	51 M	drowsiness for two months, acute hemiplegia	inhomogenously enhancing mass	R thalamus	30x50x4031.4 ml	Biopsy R frontal	Inconclusive (necrosis: GBM at craniotomy)	Y: d21	N/A	NIL	Partial success; inconclusive histology
7	55 F	scleroderma; L hemiparesis for one week	ring-enhancing lesion	R occipital WM	20x20x20 4.2 ml	Biopsy R parietal	Undifferentiated carcinoma	No	N/A	NIL	Successful
8	54 F	headache and L hemiparesis for one week	multile ring-enhancing lesions	R parietal subcortical	20x20x20 4.2 ml	Biopsy R parietal	Inconclusive (necrosis: GBM at autopsy)	Y: d21	N/A	NIL	Partial success; inconclusive histology
9	34 F	cervical carcinoma; L focal seizure and hemiparesis	cyst with enhancing wall	R parietal subcortical	35x25x25 11.5 ml	Aspiration R parietal	Squamous carcinoma	No	N/A	NIL	Successful
10	42 M	headache and vomiting, fever, L hemiparesis	ring-enhancing lesion	R centrum semiovale	20x20x25 5.2 ml	Aspiration R frontal	Abscess	Y: d4	N/A	transient L leg weakness	Successful
11	66 M	headache for many months	ring-enhancing lesion	corpus callosum, body	25x25x25 8.2 ml	Biopsy R frontal	Adenocarcinoma	No	N/A	NIL	Successful
12	27 M	headache and vomiting 6for six weeks, papilloedema	inhomogenously enhancing mass	L basal ganglia	30x50x30 23.6 ml	Biopsy L frontal	Inconclusive (malignant tumour, likely GBM)	Y: d1	Y: 10-20 mm	NIL	Partial success; inconclusive histology

13	24 M	L focal seizure	ring-enhancing lesion	R frontal cortical	15x10x10 0.8 ml	Aspiration R frontal	Parasitic cyst	Y: d5	N/A	NIL	Successful
14	0.3 M	macrocrania	inhomogenously enhancing mass	L basal ganglia	20x15x20 3.1ml	Biopsy L parietal	Inconclusive (?vascular lesion, cavernous angioma at follow-up)	Y: d1	No	NIL	Partial success; inconclusive histology
15	0.2 F	macrocrania	arachnoid cyst	quadrigeminal cistern	40x30x40 3.1 ml	Cannulation R parietal	Arachnoid cyst	Y: d1	N/A	NIL	Successful
16	59 M	confusion, headache and L hemiparesis	ring-enhancing lesion	R frontal deep WM	30x25x20 7.9 ml	Biopsy R frontal	Undifferentiated carcinoma	Y: d1	Y: <5 mm	transient drowsiness, hyperglycaemia	Successful
17	22 M	epilepsy for four years	hypodense mass with speckled cacification	R temporal WM	20x20x20 4.2 ml	Biopsy R temporal	Inconclusive (low grade glioma)	Y: d3	No	NIL	Partial success; inconclusive histology
18	49 M	R hemiparesis and aphasia	inhomogenously enhancing mass	L basal ganglia	50x50x40 52.4 ml	Biopsy L frontal	Undifferentiated carcinoma	Y: d7	N/A	NIL	Successful
19	21 M	R focal seizure and hemiparesis	hypodense mass	L parietal WM	30x30x30 14.1 ml	Biopsy L parietal	Low grade glioma	Y: 1y	N/A	anti-convulsant rash, DVT	Successful
20	20 M	AIDS with PCP pneumonia; L hemiplegia	inhomogenously enhancing mass	R basal ganglia	40x30x40 25.1 ml	Biopsy R frontal	Inconclusive (non-specific inflammatory)	Y: d1	Y: 20-40 mm	NIL	Partial success; inconclusive histology
21	2.5 F	macrocrania and shunt dysfunction	isolated ventricle	R lateral ventricle, body	50x40x40 41.9 ml	Cannulation R frontal	Multiloculated hydrocephalus	Y: d1	N/A	NIL	Successful
22	22 M	dementia; headache for three months	inhomogenously enhancing mass	corpus callosum, splenium	50x50x50 65.5 ml	Biopsy R parietal	GBM	Y: d3	No	NIL	Successful
23	44 M	cognitive decline with L hemiparesis	multiple ring-enhancing lesions	R subcortical WM	30x30x30 14.1 ml	Biopsy R parietal	Adenocarcinoma	No	N/A	NIL	Successful
24	70 M	L hemiparesis	inhomogenously enhancing mass	R fronto-parietal subcortical	30x30x30 14.1 ml	Biopsy R frontal	Adenocarcinoma	No	N/A	NIL	Successful
25	47 F	cognitive decline with headache	hypodense mass	L parietal subcortical	30x40x30 18.9 ml	Biopsy R parietal	Actinomycosis	Y: d1	Y: <5 mm	NIL	Successful
26	31 M	AIDS; generalized seizure and L hemiparesis	ring-enhancing lesion	R lateral ventricle trigone	20x25x20 5.2 ml	Aspiration R parietal	Amoebic abscess	Y: d3	N/A	NIL	Successful
27	35 F	L focal seizures and hemiparesis	ring-enhancing lesion	R fronto-parietal subcortical	15x20x20 3.1 ml	Biopsy R parietal	Anaplastic glioma	Y: d1	Y: 5-10 mm	transient L leg weakness	Successful
28	34 F	numbness L foot	multiple ring-enhancing lesions	R parietal deep WM	10x10x10 0.5 ml	Biopsy R parietal	Non-diagnostic (normal brain)	Y: d1	Y: 5-10 mm	NIL	Failed; system error

29	66 M	mild headache	ring-enhancing lesion	R parietal subcortical	15x15x15 1.8 ml	Biopsy R occipital	GBM	Y: d1	No	NIL	Successful
30	49 M	pneumonectomy for lung Ca 6 months ago; R focal seizures and hemiparesis	inhomogenously inhancing mass	L parietal cortical, parafalcine	20x30x20 6.3 ml	Craniotomy L parietal, following biopsy	Adenocarcinoma	Y: d1	No	NIL	Successful
31	50 M	R focal seizures and hemiparesis	ring-enhancing lesion	L fronto-parietal deep WM	20x35x30 11.0 ml	Aspiration L frontal	Abscess	Y: d4	N/A	NIL	Successful
32	74 M	PTB 1 year ago; R focal seizures and hemiparesis	ring-enhancing lesion	L fronto-parietal subcortical	25x12x15 2.4 ml	Aspiration L frontal	Abscess	Y	N/A	anti-convulsant rash	Successful
33	21 M	headache and vomiting followed by seizure; subsequent L hemiparesis	ring-enhancing lesion	R fronto-parietal subcortical	20x20x20 4.2 ml	Aspiration R frontal	Abscess	Y	N/A	local wound sepsis	Successful
34	35 M	headache and vomiting, for 4 weeks; R hemiparesis and dysphasia	ring-enhancing lesion	L fronto-parietal subcortical	30x30x30 14.1 ml	Biopsy L frontal	Adenocarcinoma	Y: d1	Y: 5-10 mm	delayed waking	Successful
35	56 M	HIV+; L focal seizures and hemiparesis	multiple enhancing lesions	R parietal cortical, parafalcine	20x20x20 4.2 ml	Biopsy R parietal	GBM	Y: d1	Y: 5-10 mm	NIL	Successful
36	57 M	smoker with a lung mass, headache and R parietal syndrome	ring-enhancing lesion	R centrum semiovale	40x40x40 33.5 ml	Biopsy R parietal	Adenocarcinoma	No	N/A	NIL	Successful
37	65 M	generalized seizures and L hemianopia	inhomogenously enhancing mass	R occipital WM	20x20x15 3.1 ml	Craniotomy R occipital following biopsy	GBM	Y: d1	No	anti-convulsant rash	Successful
38	67 F	hypertension; episodes of loss of consciousness and R focal seizures	enhancing mass	L occipital cortical	25x25x20 6.5 ml	Biopsy L occipital	Anaplastic glioma	Y: d1	Y: 5-10 mm	NIL	Successful
39	4 M	1 month progressive L hemiparesis	enhancing mass with cystic component	R midbrain	30x20x20 6.3 ml	Biopsy R frontal	JPA	Y: d1	Y: 5-10 mm	NIL	Successful
40_1	15 F	headache for 9 months, then hemiparesis L and bulbar symptoms	inhomogenously enhancing mass	R midbrain	25x20x15 3.9 ml	Biopsy R frontal	Anaplastic glioma	Y: d1	Y: 5-10 mm	NIL	Successful
40_2	16 F	2nd procedure- worsening L hemiparesis with a new lesion	inhomogenously enhancing mass	R inferior frontal cortex	25x20x15 3.9 ml	Biopsy R frontal	Anaplastic glioma	Y: d1	Y: 5-10 mm	NIL	Successful
41	49 F	smoker with suspicious CXR; focal seizures	multiple enhancing lesions	L frontal cortical	15x15x10 1.2 ml	Biopsy L frontal	Adenocarcinoma	Y: d1	Y: 5-10 mm	NIL	Successful

42_1	19 M	thalamic pain syndrome with L hemiparesis	inhomogenously enhancing mass	R thalamus	12x12x10 0.8 ml	Biopsy R frontal	Germ cell tumour	Y: d1	Y: <5 mm	NIL	Successful
42_2	20 M	2nd procedure- new onset gaze palsy	inhomogenously enhancing mass	R thalamus	10x10x10 0.5 ml	Biopsy R frontal	No malignancy	Y: 6mo	N/A	NIL	Successful
43	46 M	L hemiplegia for 6 months	inhomogenously enhancing mass	R basal ganglia	40x30x30 18.9 ml	Biopsy R parietal	GBM	Y: d0	Y: <5 mm	NIL	Successful
44	26 F	headache 3 months, papil-loedema	inhomogenously enhancing mass	corpus callosum, genu	40x30x30 18.9 ml	Biopsy L frontal	Anaplastic glioma	Y: d1	No	NIL	Successful
45	15 F	headache; previous crani-opharyngioma	calcified cyst wall	suprasellar	50x50x50 65.5 ml	Cannulation R frontal	Craniopharyngioma	Y	N/A	NIL	Successful
46	48 M	headache for six months; cognitive decline and L neglect	multiple enhancing lesions	R frontal subcortical	20x10x10 1.0 ml	Biopsy R frontal	GBM	Y: d7	N/A	NIL	Successful
47	36 M	smoker; headache for 1 month followed by aphasia and R hemiparesis	ring-enhancing lesion	R frontal deep WM	20x15x20 3.1 ml	Aspiration R frontal	Infarct	Y	N	NIL	Successful
48_1	5 M	visual deterioration follow-ing minor head injury	calcified cyst wall	suprasellar	35x30x30 16.5 ml	Cannulation R frontal	Craniopharyngioma	Y	N/A	failed to penetrate cyst wall	Failed; surgeon error
48_2	5 M	2nd procedure- misplace-ment of catheter	calcified cyst wall	suprasellar	35x30x30 16.5 ml	Cannulation R frontal	Craniopharyngioma	Y	N/A	marked DI	Successful
49	33 F	dental surgery; severe headache 1 week later	ring-enhancing lesion	R frontal deep WM	25x20x20 5.2 ml	Aspiration R frontal	Abscess	Y: d2	N/A	NIL	Successful
50	11 F	NF Type 1; longstanding visual deterioration and L hemiparesis	enhancing mass	L thalamus	30x30x20 9.4 ml	Biopsy L occipital	JPA	Y: d1	No	NIL	Successful
51	30 M	headache 1 week after assault	ring-enhancing lesion	R frontal deep WM	10x10x10 0.5 ml	Aspiration R frontal	Abscess	Y: d4	N/A	NIL	Successful
52	48 M	bronchiectasis; hemiparesis L for 3 months	ring-enhancing lesion	R parietal deep WM	25x25x20 6.5 ml	Aspiration R parietal	Abscess	Y: d2	N/A	NIL	Successful
53	40 M	hypertension; headache 3 months; cognitive decline	inhomogenously enhancing mass	corpus callosum, splenium	50x35x20 18.3 ml	Biopsy L parietal	GBM	No	N/A	NIL	Successful
54	73 F	confusion and L neglect	multiple inhomog-enously enhancing lesions	R frontal cortical	30x30x30 14.1 ml	Biopsy R frontal	GBM	No	N/A	NIL	Successful
55_1	14 F	recurrent hydatid disease with hydrocephalus	isolated temporal horn	L lateral ventricle, temporal horn	30x30x30 14.1 ml	Cannulation L temporal	Hydrocephalus	Y	N/A	NIL	Successful

55_2	14 F	2nd procedure for insertion of shunt	isolated temporal horn	L lateral ventricle, temporal horn	20x20x20 4.2 ml	Cannulation L occipital	Hydrocephalus	Y	N/A	NIL	Successful
56	21 F	cognitive decline 1 month; hydrocephalus	inhomogenously enhancing mass	suprasellar, hypothalamic	30x40x30 18.9 ml	Biopsy R frontal	GBM	Y: d1	No	NIL	Successful
57	74 F	cognitive decline 6 months	inhomogenously enhancing cystic/ solid mass	R temporal cortical	40x40x40 33.5 ml	Craniotomy R temporal	GBM	Y	N/A	transient confusion; anticonvulsant rash	Successful
58	36 F	epilepsy 15 years followed by hemiparesis R; craniotomy for tumour in 1996, central neurocytoma, recurrence	inhomogenously enhancing mass	L frontal cortical	30x30x30 14.1 ml	Biopsy L frontal	Oligo-astrocytoma	Y: d2	Y: 5-10 mm	NIL	Successful
59	31 F	focal seizures for 3 months followed by R hemiparesis for 10 days	inhomogenously enhancing mass	L parietal deep WM	35x50x40 36.7 ml	Biopsy L parietal	Anaplastic glioma	Y: d3	Y: 5-10 mm	transient weakness R leg	Successful
60	16 F	previous craniotomy for craniopharyngioma; visual deterioration and headache	enhancing calcified cyst wall	suprasellar	15x10x10 0.8 ml	Cannulation R frontal	Craniopharyngioma	Y	N/A	NIL	Successful
61_1	50 M	COAD, mild hemiparesis L and dysphasia	multiple ring-enhancing lesions	R thalamus	20x25x20 5.2 ml	Aspiration R frontal	Abscess	Y	N/A	NIL	Successful
61_2	50 M	2nd procedure to retap abscess	multiple ring-enhancing lesions	R thalamus	20x25x20 5.2 ml	Aspiration R frontal	Abscess	Y	N/A	NIL	Successful
62	42 M	headache for 1 month following MVA	inhomogenously enhancing mass	L temporal WM	40x40x20 16.8 ml	Biopsy R frontal	Anaplastic glioma	Y: d21	N/A	NIL	Successful
63	57 F	cognitive decline over 1 month	inhomogenously enhancing mass	corpus callosum, genu	30x30x30 14.1 ml	Biopsy R frontal	Anaplastic glioma	Y: d1	No	NIL	Successful
64	70 M	seizures	inhomogenously enhancing mass	L frontal cortex	30x20x20 6.3 ml	Biopsy L frontal	Anaplastic glioma	Y: d1	Y: <5 mm	NIL	Successful
65	43 F	headache for 2 months, collapse and confusion	inhomogenously enhancing mass	L frontal deep WM	20x30x25 7.9 ml	Biopsy L frontal	Adenocarcinoma	No	N/A	NIL	Successful
66	20 F	dysmorphic, no diagnosis; poor vision and R hemianopia for 4 years	inhomogenously enhancing mass	L occipital cortical	40x50x40 41.9 ml	Biopsy L occipital	Ependymoma	Y: d2	No	NIL	Successful
67	14 M	Grade 3 spinal cord astrocytoma June 1997; headache	enhancing mass	lateral ventricle, frontal horn	10x10x10 0.5 ml	Biopsy L frontal	Non-diagnostic Normal brain and choroid plexus	Y: 3 w	N/A	NIL	Failed; surgeon error

68	24 M	R focal seizures for 6 years	cystic mass	L frontal deep WM	20x30x20 6.3 ml	Aspiration L frontal	Cysticercosis	Y: d2	N/A	NIL	Successful
69	45 F	R focal seizures and cognitive decline	inhomogenously enhancing mass with dense calcification	L parietal deep WM	15x30x30 7.1 ml	Biopsy L parietal	Oligodendroglioma	Y: 3 months	N/A	phenytoin rash	Successful
70	82 M	IHD and COAD; mild hemiparesis R with cognitive decline	avidly enhancing mass	L basal ganglia	30x40x40 25.1 ml	Biopsy L frontal	High grade non-Hodgkins Lymphoma	Y: d0	Y: <5 mm	NIL	Successful
71_1	49 F	deteriorating vision for 1.5 y and headache for 1 y	cystic mass	suprasellar	20x30x30 9.4 ml	Cannulation L frontal	Craniopharyngioma	Y: d1	N/A	NIL	Successful
71_2	49F	2nd procedure to reposition catheter	cystic mass	suprasellar	20x30x30 9.4 ml	Cannulation L frontal	Craniopharyngioma	Y: d1	N/A	NIL	Successful
72	44 F	drowsiness following 1 month of headache and vomiting	large inhomogenous enhancing mass	R tempero-parietal deep WM	xx	Biopsy R parietal	Anaplastic glioma	Y: d5	N/A	hypo-natremia and drowsy for two days. Died d5.	Successful
73	25 F	acute raised intracranial pressure; emergency drainage of cyst in East London	cystic mass	suprasellar	40x60x40 50.3 ml	Cannulation R frontal	Craniopharyngioma	Y: d1	N/A	delayed waking	Successful
74	43 M	oligodendroglioma excised 1993, followed by RT. Worse seizures with dysphasia	enhancing mass	L parietal subcortical	30x40x30 18.9 ml	Biopsy L frontal	Oligoastrocytoma	Y: d1	No	NIL	Successful
75_1	32 F	Pulmonary TB 5 y ago; focal seizures	ring-enhancing cystic lesion	L parietal cortical	30x30x25 11.8 ml	Biopsy L parietal	Non-diagnostic (inflammatory)	Y: d1	Y: <5 mm	NIL	Failed; surgeon error
75_2	32 F	2nd procedure- first non-diagnostic	ring-enhancing cystic lesion	L parietal cortical	30x30x25 11.8 ml	Biopsy L parietal	Non-diagnostic (oedematous brain and thrombus)	Y: d0	Y: >40 mm	postoperative haematoma requiring urgent craniotomy	Failed; surgeon error
76	6 F	headache and deteriorating vision	enhancing calcified cyst wall	suprasellar	15x20x30 4.7 ml	Cannulation R frontal	Craniopharyngioma	Y	N/A	NIL	Successful
77_1	29 F	headache for 6 months, hemiparesis R 4 mo	enhancing mass	corpus callosum, genu and L frontal deep WM	40x30x40 25.1 ml	Biopsy L frontal	Non-diagnostic normal brain	Y: d1	No	NIL	Failed; incorrect use of system

77_2	29 F	2nd procedure- first non-diagnostic	enhancing mass	corpus callosum, genu and L frontal deep WM	40x30x40 25.1 ml	Biopsy L frontal	Non-diagnostic high grade tumour on smear	No	N/A	NIL	Failed; incorrect use of system
77_3	29 F	3rd procedure- 2nd non-diagnostic	enhancing mass	corpus callosum, genu and L frontal deep WM	40x30x40 25.1 ml	Biopsy L frontal	Anaplastic glioma	Y: d1	No	NIL	Successful
78	6 F	headache and vomiting 1 month, polydipsia and short stature	calcified cyst wall	suprasellar	15x20x20 3.1 ml	Cannulation R frontal	Craniopharyngioma	Y	N/A	NIL	Failed; incorrect use of system
79_1	52 F	PTB and NIDDM; weight loss, confusion and incontinence for 6 months; GCS 10/15 with mild L hemiparesis	inhomogenously enhancing mass	corpus callosum, genu	20x30x20 6.3 ml	Biopsy R frontal	Non-diagnostic	Y: d1	Y: 5-10 mm	NIL	Failed; incorrect use of system
79_2	52 F	2nd procedure- first non-diagnostic	inhomogenously enhancing mass	corpus callosum, genu	20x30x20 6.3 ml	Biopsy R frontal	Non-diagnostic	Y: d1	No	NIL	Failed; incorrect use of system
79_3	52 F	3rd procedure- 2nd non-diagnostic	inhomogenously enhancing mass	corpus callosum, genu	20x30x20 6.3 ml	Biopsy R frontal	Non-diagnostic (?)	No	N/A	NIL	Partial success; inconclusive histology
80_1	13 M	headache and deteriorating vision	solid tumour with enhancing and calcified cyst wall	suprasellar	20x20x25 5.2 ml	Cannulation R frontal	Craniopharyngioma	Y: d0	Y: large SAH	intra-operative haemorrhage requiring craniotomy	Failed; abandoned due to haemorrhage
80_2	13 M	2nd procedure- first abandoned due to haemorrhage	solid tumour with enhancing and calcified cyst wall	suprasellar	20x20x25 5.2 ml	Cannulation L frontal	Craniopharyngioma	Y	N/A	NIL	Successful
81	62 M	seizures and confusion	inhomogenously enhancing mass	L temporal subcortical	35x20x30 11.0 ml	Biopsy L temporal	GBM	Y: d1	No	NIL	Successful
82	53 F	headache with deteriorating vision over 1 year, personality change	cystic/ solid tumour with enhancing wall	suprasellar	35x30x35 19.3ml	Cannulation R frontal	Craniopharyngioma	Y	N/A	NIL	Successful
83	61 F	headache for 1 week	ring-enhancing lesion	R parietal deep WM	30x25x20 7.9 ml	Biopsy R parietal	Anaplastic glioma	Y: d1	Y: <5 mm	NIL	Successful
84	49 M	headaches and vomiting, seizures	ring-enhancing mass, marked oedema	L posterior temporal cortical	30x30x30 14.1 ml	Biopsy L temporal	GBM	Y: d1	Y: 5-10 mm	NIL	Successful

85	49 M	L hemiparesis with deteriorating level of consciousness	inhomogenously enhancing mass; multifocal leucoencephalopathy	R basal ganglia (caudate)	30x25x30 11.8 ml	Biopsy R frontal	High grade B cell Lymphoma	Y: d8	N/A	NIL	Successful
86	8 M	headache for 2 weeks, L hemiparesis for 1 week	inhomogenously enhancing mass	R basal ganglia (caudate)	35x35x30 19.3 ml	Biopsy R frontal	Infart (vasculitic)	Y: d1	No	NIL	Successful
87	14 F	bilateral shunts and craniotomy 1995; headache with mild R hemiparesis	cystic mass with calcified/ enhancing wall	suprasellar	30x40x30 18.9 ml	Cannulation L frontal	Craniopharyngioma	Y	N/A	NIL	Successful
88	4 M	macrosomia with developmental delay; L focal sz with progressive hemiparesis	multiple enhancing lesions	R basal ganglia (thalamus)	50x45x35 41.3 ml	Biopsy R frontal	JPA	Y: d1	No	NIL	Successful
89_1	35 M	headache 1 month	multiple enhancing lesions	R temporal deep WM	20x15x15 2.4 ml	Aspiration R temporal	Abscess	Y	N/A	NIL	Successful
89_2	35 M	2nd procedure- reaccumulation of abscess	multiple enhancing lesions	R temporal deep WM	15x15x10 1.2 ml	Aspiration R temporal	Abscess	Y	N/A	NIL	Successful
90	1.5 F	blind	cystic mass	suprasellar	35x40x40 29.3 ml	Cannulation R frontal	Craniopharyngioma	Y	N/A	NIL	Successful
91	37 F	headache and vomiting	inhomogenously enhancing mass	corpus callosum, genu	40x30x30 18.9 ml	Biopsy R frontal	Anaplastic glioma	Y: d0	No	phenytoin rash	Successful
92	6 M	headache and diabetes insipidus	cystic mass with calcified/ enhancing wall	suprasellar	40x35x35 25.7 ml	Cannulation L frontal	Craniopharyngioma	Y	N/A	transient DI	Successful
93_1	29 F	SLE, CRF and hypertension; focal seizures and R hemiparesis	multiple ring-enhancing lesions	L frontal cortical	15x15x20 2.4 ml	Aspiration R frontal	Abscess	Y	N/A	NIL	Successful
93_2	30 F	2nd procedure- abscess at a second site	multiple ring-enhancing lesions	L frontal cortical	15x15x20 2.4 ml	Aspiration L frontal	Abscess	Y: d2	N/A	NIL	Successful
94	58 F	Weight loss, headache, syncope and L leg weakness.	multiple inhomogenously enhancing lesions	R frontal cortical	30x30x25 11.8 ml	Biopsy R frontal	Adenocarcinoma	Y: d1	No	mild dysphasia, phenytoin rash	Successful

95	8 M	failure to thrive for 6 months, headache for 1 month; bilateral shunts and craniotomy 4 months previously. New onset L hemiparesis.	irregular calcified suprasellar enhancing mass with R temporal cyst	suprasellar	25x40x35 18.3 ml	Cannulation R frontal	Craniopharyngioma	Y	N/A	transient DI	Successful
96	39 M	seizures for 2 years, L sensory symptoms with slurred speech and confusion	low density mass with little enhancement	R temporal deep WM	40x50x30 31.4 ml	Biopsy R temporal	Low grade glioma	Y: d1	Y: 10-20 mm	NIL	Successful
97	42 F	Hypertension; seizures for 1 year with recent headache and confusion	inhomogenously enhancing mass	R fronto-parietal subcortical	xx	Biopsy R frontal	Anaplastic glioma	Y: d1	No	NIL	Successful
98	53 M	leg weakness following a fall	inhomogenously enhancing mass	L fronto-parietal subcortical	15x15x15 1.8 ml	Biopsy L frontal	Undifferentiated carcinoma	Y: d1	No	NIL	Successful
99	61 M	NIDDM and hypertension; unsteady gait for 2 years with cognitive decline and L hemiparesis for 3 months	multiple hyperdense enhancing lesions	R parietal deepWM	25x20x20 5.2 ml	Biopsy R parietal	High grade B cell Non-Hodgkins Lymphoma	Y: d0	Y: 5-10 mm	NIL	Successful
100	65 F	personality change and incontinence, L hemiparesis	inhomogenously enhancing mass	corpus callosum, genu, R frontal deep WM	50x40x40 41.9 ml	Biopsy R frontal	GBM	Y: d1	No	NIL	Successful

Appendix II

CT data sheet

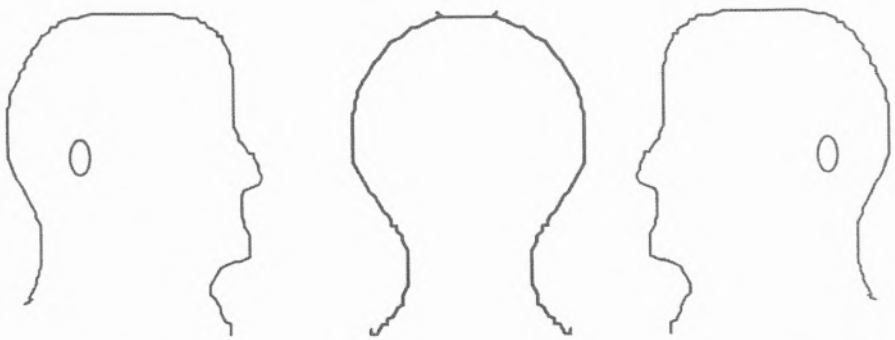
PATIENT FORM FOR CT SCAN DATA TO SET THREE LEGGED STOOL

Patient's Label	

CT scan file name	
CT scan date	
CT scan proforma e.g. prone	
PC file name (less than 5char's)	

	X	Y	Z	Scan No.	Slice Width
Lesion 1					
Lesion 2					
Entry					
Leg 1					
Leg 2					
Leg3					

Data logger's name	



	X	Y	Z
Phantom Settings			

Appendix III

The Cape Town Stereotactic Pointer: Standard components supplied by Fibreter and current protocol for use

- Halo
  - CT halo
  - MRI halo

- Tripod components
  - Tripod base
  - Tripod pillar
  - Tripod arm
  - Tripod knob and collar
  - Tripod screwdriver (Allen key)
  - Tripod support block
  - Instrument guide sleeve
  - Cut-off instrument guide sleeve
  - 2.5 mm perpendicular pointer
  - 3.2 mm perpendicular pointer

- Setting Phantom
  - Burr-hole indicator arm

- Biopsy and other Instruments
  - 2.5mm side-cutting biopsy needle
  - 2.5mm aspiration needle
  - 4.2mm haematoma aspirator

- Instrument case
  - Carrying case

The Cape Town Stereotactic Pointer: Protocol for use

Through repeated use, a simplified technique evolved which entails 4 stages:

2i Application of the Halo

The circular halo serves 2 purposes:

1. it contains the *fiducials,* which are three radiopaque ball bearings, 2mm in diameter, which are macroscopically visible and also seen on the CT image

2. it serves as the *platform* upon which the tripod (stereotactic pointing device) will be mounted, having three small holes on the upper surface which securely house the three feet of the tripod.

It is worth noting that the fiducials are not located exactly at the holes occupied by the feet of the tripod, even though each fiducial is referred to as "leg 1", "leg 2" and "leg 3". As each halo is manufactured to exactly the same specifications, the calibration data in the software corrects for this offset. The halo must not be able to move during the CT scan or, even more importantly, during the surgical procedure. As it also serves as the external reference system, generating co-ordinates, which are determined using the software intrinsic to the CT scanner, it is absolutely essential that the halo be securely fixed to the patient's head.

This is achieved by suturing the halo to the scalp using 2/0 silk. The hair need not be shaved at this point although the scalp and hair is cleaned with the solutions used for preoperative skin preparation (in our case, chlorhexidine shampoo followed by chlorhexidine in 70% alcohol). Important considerations in selecting the location for the halo include:

- it should be situated in the optimal position for a convenient and safe trajectory to the intracranial target from a burr hole located in the centre

- it must be positioned so that it is stable and unable to rock from side to side

Three small feet projecting from the inferior surface of the halo help with stabilization and it is secured with four or five sutures of 2/0 silk distributed more or less evenly around the circumference. If the suture is passed through one of the four perforations in the halo one

achieves a snug fit; an alternative method is to secure the halo with self-tapping screws inserted into the skull.

With an awake patient, it is necessary to precede suturing with infiltration of local anaesthetic once one has determined where the sutures should be placed. It is important that sufficient time be allowed to elapse, not only to enable the anaesthetic to work but also to allow the agent to dissipate in the tissues so that there is not a large skin bleb that may reduce the stability of the halo. Needless to say, careful explanation before and constant encouragement during the procedure go a long way towards helping the patient to tolerate this.

As the three fiducials are indistinguishable on the CT scan image, it is important to take note of the orientation of the halo and hence the fiducials. It is recommended that one routinely use a particular convention, for example, our usual practice is to rotate the halo so that the middle fiducial (termed "leg 2" although this is not strictly speaking correct) is closest to the midline of the patient's head- this diminishes the chances of misidentification of the fiducials. Other helpful practices include taking note of the sequence in which the fiducials will be imaged during the scan and drawing a simple diagram which can be referred to during the scan is also helpful.

Although the prototype halo was manufactured from transparent polycarbonate, European Union rules required that it be manufactured from a material that complied with the US Pharmacopeia Class VI standard and since 2002 the halo has been made from Ultem 1000 plastic (polyetherimide) [PJ Mundell, personal communication]. The fiducials however remain visible and it is essential that the halo not be autoclaved.

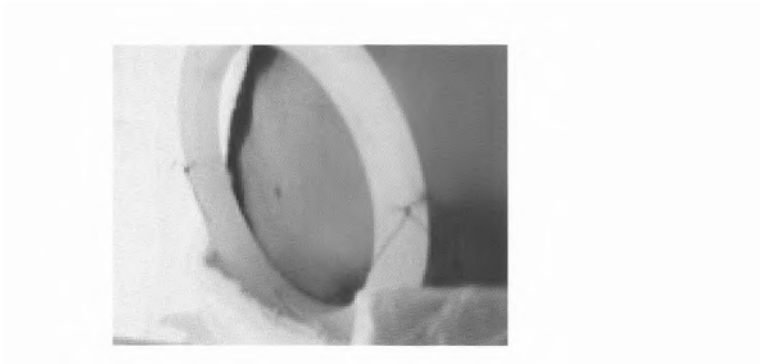


Figure AI: low power laser confirming CT slice is coincident with fiducial

2.2 CT Scan

This is the data acquisition stage and is easily adapted to local radiological practice. In essence, one needs only four axial images, namely those through the three fiducials and one through the target. In order to optimize the selection of the target however, usually a series of scans is planned through the region of interest. Most cerebral lesions that require biopsy or aspiration will enhance and administration of intravenous contrast such as Omnipaque® is very helpful in delineating the pathological area.

The standard head holder may be used, which is preferable to the patient lying with the head on the table itself as the holder tends to restrict head movement, which is further discouraged by placing a strip of masking tape lightly across the brow. The patient is positioned with the halo uppermost- not only does this reduce scalp distortion, but it also replicates the most likely operative position and therefore diminishes brain shift should one operate in a different position.

The gantry must not be angled. The scanning protocol then depends on the capabilities of the particular scanner. The most common practice at present is to plan a helical scan from the fiducials down to the region of interest taking two mm thick contiguous slices. This is certainly the quickest technique with most current helical scanners taking no more than a minute or so; such scanners are not always found in centres where the CTSP is used.

An alternative is to plan the slices from the lateral or anteroposterior surview or "scout" view; should one plan individual slices, each should be 1 mm thick for optimal accuracy. Using this approach may be preferable should one want to limit the amount of radiation and is particularly appealing in children, who for that matter are usually anaesthetized anyway so doing the scan very rapidly is not that necessary. Should there be any concern, the first fiducial imaged should be scanned again and this will immediately show if there has been any interval change in position.

An efficient sequence is to scan through the area of interest and then determine which slices are optimal for selecting a target. A sequence of four consecutive scans is then planned, one through each fiducial and one through the previously selected "target" area. It is usually straightforward to obtain these images in a very short time — no more than a couple of minutes. It is almost always possible to get the patient to lie still for this period and provided these four successive images were obtained without movement, a highly reliable data set is obtained.

If more than one intracranial target is required (for example, biopsies from two different regions of a tumour), the appropriate images must be obtained at this stage.

The fiducials must be clearly seen; simply seeing the edge is not acceptable. The software intrinsic to the CT scanner enables one to readily obtain x and y co-ordinates for each fiducial by superimposing the grid and moving the cursor on the display screen.

Movement of the bed on which the patient lies is very precisely calibrated with the bed position appearing on each slice; this figure serves as the z co-ordinate. Two points are worth emphasizing:

- do not attempt to move the Cartesian grid on the screen or alter the image size after scanning as this will render all values meaningless

- The x and y co-ordinates are usually given in millimeters while the table position is in centimeters. This necessitates multiplication of the table position by ten as all the stereotactic co-ordinates must be entered as millimeters.

It is also important to check that both the (table position) Z axis and the X and Y co-ordinates on the screen are in the same units, as some manufacturers display one in centimeters and the other in millimeters.

2.3 Calculation of Stereotactic Co-ordinates

Upon completion of the scan, the neurosurgeon should be satisfied that the co-ordinates look intuitively correct. Invariably the x-axis runs horizontally and the y-axis vertically with the origin of the axes in the centre of the image and x=0 and y=0 at the intersection of the two axes; x is negative to the left of the origin and y is negative below the origin. In other words, a fiducial located in the upper right quadrant has positive values for both x and y, while one located in the lower left quadrant has negative values for both x and y.

The x-, y- and z- co-ordinates are then obtained for at least one and preferably two intracranial targets. As previously discussed, there is substantial consensus that the highest diagnostic yield is from enhancing regions and this is therefore the area to target. These four sets of x-, y- and z- co-ordinates are all that one needs in order to perform the stereotactic procedure.

The CTSP software has been written in an easily used Windows program, which is licensed, to FibretekTM. The first step is to enter the salient patient details as a new folder, which is saved with the suffix ".pha".

The second step is to select "enter co-ordinates" from the drop-down menu and enter these four sets of three co-ordinates taking great care to do this in the correct order. The importance of vigilance at this point cannot be over-emphasized and in general it works best to have one person read out the values, taking care to state which values are negative, with a second person entering the data. Once completed, this is then read back off the screen.

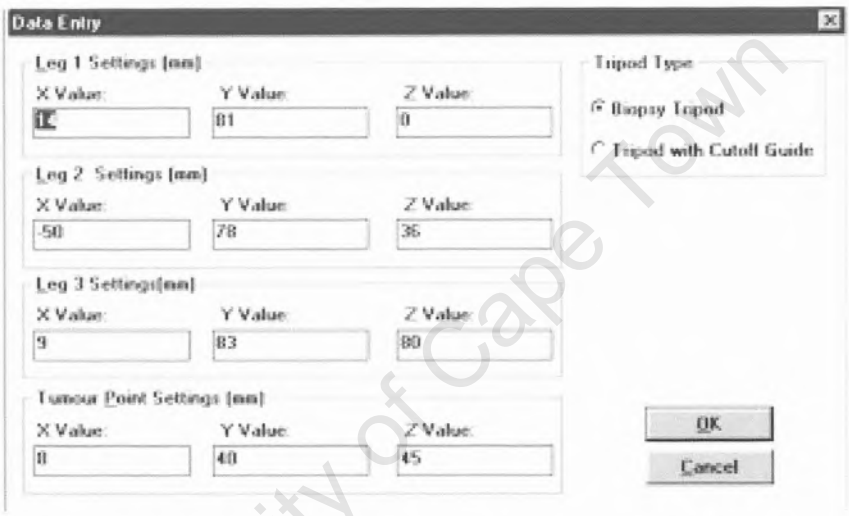


Figure A2: Screenshot of the data entry page (Picture credit: Mr PJ Mundell).

If the data is correct, click "OK" and a data block is displayed which indicates the differences between the co-ordinate values for the fiducials as measured on the scan and the calibrated values.

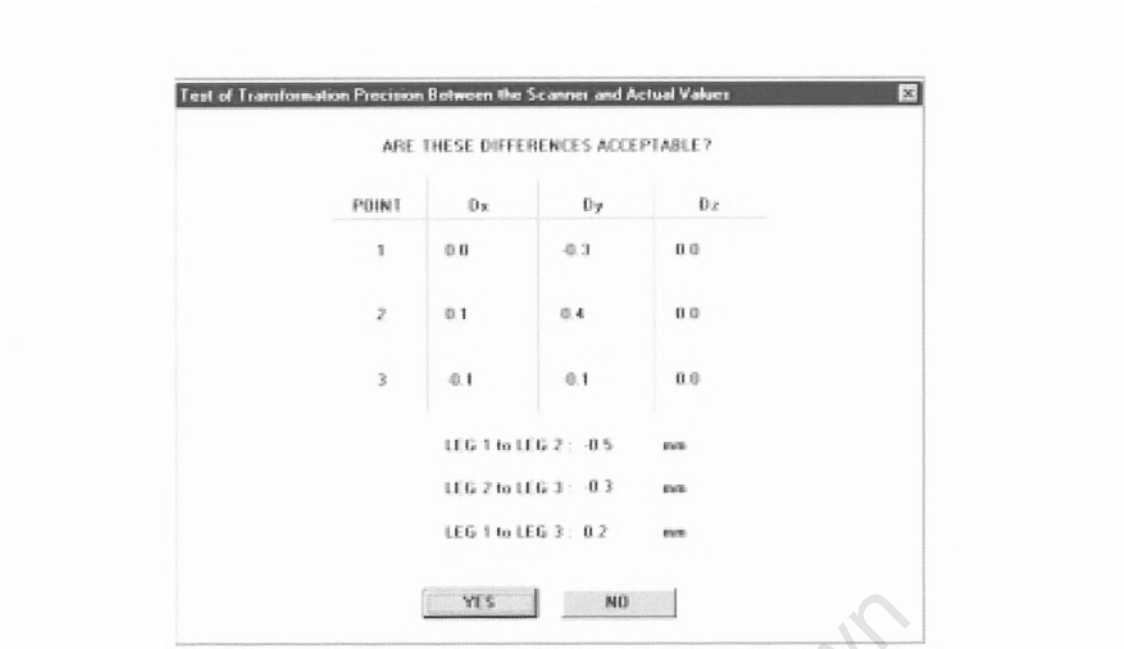


Fig A3: Screenshot of the test of transformation precision (Picture credit: Mr PJ Mundell).

This test of transformation precision warrants detailed explanation. As the distances between the fiducials housed in the halo are fixed, this enables one to establish how accurate the CT data is. The CTSP software compares the distances from "leg 1 to leg 2", "leg 1 to leg 3" and "leg 2 to leg 3" and reveals whether the data is reliable. This enables the surgeon to make a judgment call; should the target be deep seated, accepting an error of greater than 1mm would be unwise, while a slightly greater margin may exist should the target be large or superficial.

If the test of transformation precision shows an unacceptable degree of error, the first step is to check that the data has been entered correctly. Should that not be the problem, each step of the procedure is carefully reviewed and the calibration data is checked against the printout supplied with the unit to ensure that this has not been altered inadvertently. If the problem persists, the most likely explanation is that there was movement during the scan and this then has to be repeated.

If this is accepted, click "Yes" and the phantom settings for x, y and z will be displayed in millimeters and these are then transcribed by adjusting the setting phantom target block in all three axes.

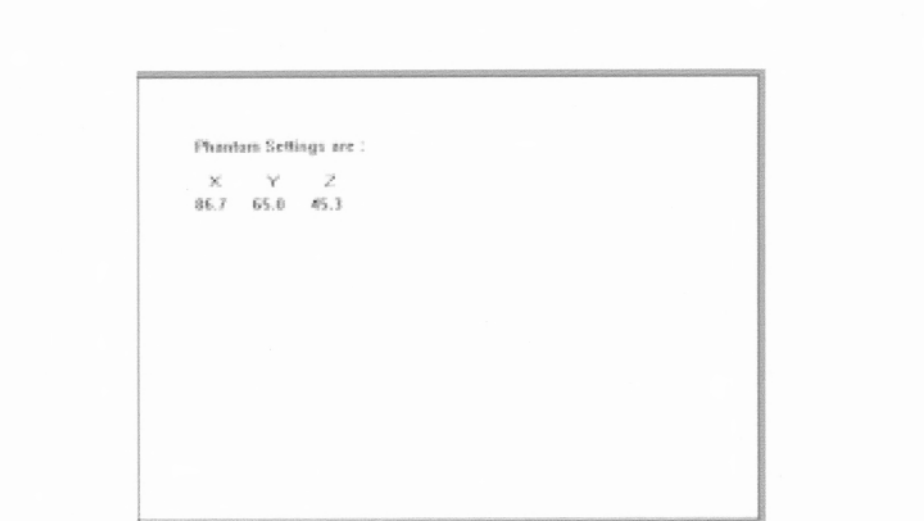


Figure A4: Screenshot of the Target co-ordinates for the 3D Phantom (Picture credit: Mr PJ Mundell).

Once the target co-ordinates have been determined, the tripod is then set on the correct trajectory using the 3D phantom; a probe or pointing rod is passed through the instrument channel to enable one to establish this trajectory (Figure A5). It is important to set the trajectory using the following sequence:

1. loosen the clamping knob on the post as well as the two screws on either side of the perpendicular plates holding the instrument guide
2. lightly tighten the screw on the inferior plate such that it is "finger tight"
3. insert the pointing rod through the instrument guide; once one is happy with the trajectory, tighten the clamping knob on the post, which will secure the horizontal arm in place
4. lastly, tighten the screw on the superior plate using the Allen key
5. the trajectory is now securely set
6. the depth is set by gently tightening the depth stop at the required position on the pointing rod or biopsy needle

It is worthwhile doing this prior to moving the patient out of the radiology department as this enables one to perform an intuitive check by coupling the tripod to the halo as most neurosurgeons will have a good idea of where they expect the lesion to be. Should the trajectory look to be on target, the patient proceeds to the operating theatre.

Figure A5: The tripod mounted on the 3D Phantom (Picture credit: Mr PJ Mundell).

The final step entails saving the data set to the ".pha" file created at the outset, to enable later retrieval in theatre or for audit or research purposes. Although at one time a printout was also generated in order to set the tripod (Figure A6), this is no longer essential, but it does however serve as useful documentation.

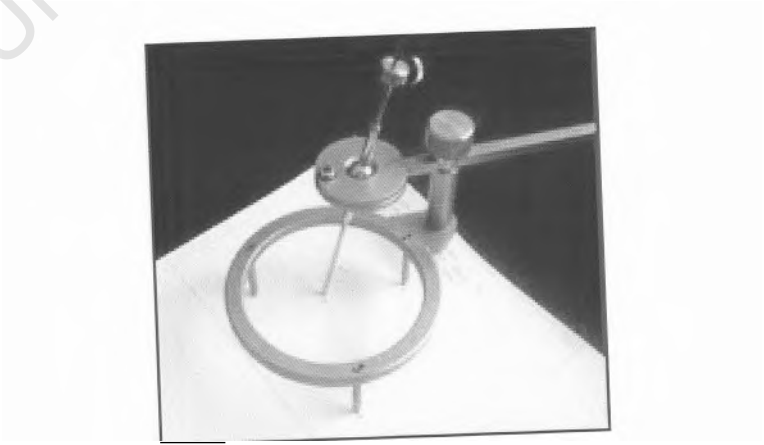


Figure A6: The tripod positioned on the setting diagram (Picture credit: Mr PJ Mundell).

2.4 Operative procedure

The phantom, tripod, biopsy needles and other accessories need to be autoclaved but there is enough time to attend to this while the patient is being anaesthetized; the tripod is mounted on a small autoclavable platform, which prevents it toppling over. Ideally the screws on the setting phantom should be loosened prior to autoclaving to avoid possible damage due to the high temperature and then re-set once the instruments have cooled sufficiently.

The patient may be operated on under general or local anaesthesia. A single dose of antibiotic is given intravenously at induction and steroids and anticonvulsants administered as appropriate. The patient's head is positioned with the halo uppermost and great care taken to ensure that there is no shift due to distortion of the scalp. The surgical site, including the halo, is prepped in the usual fashion following which the drapes are sited and a sterile adhesive drape then gently applied once the alcohol has evaporated and the halo is dry. The technique used for this is important- it is best to first apply the adhesive drape in the centre and then gently tuck it around the inner circumference before folding it over the edge of the halo and onto the surrounding scalp and drapes. Done correctly, this greatly diminishes the potential for any movement of the halo during surgery.

Ideally the surgical site will be in the centre of the halo; the scalp is infiltrated with a mixture of local anaesthetic and a vasoconstrictor (Marcaine® and Por-8®). Our preference has been to use a burr-hole so the cortical surface can be inspected to avoid lacerating a vessel, utilizing a self-retaining retractor positioned to avoid scalp distortion.

Prior to opening the dura, it is helpful to replicate the position of the burr-hole on the setting phantom in order to ensure that the appropriate trajectory is set- this is easily done with the help of the burr-hole guide. The tripod is set using the vertical guide and placed on the halo; the pointing rod is then advanced until the tip is in the centre of the burr-hole and the setting clamp tightened. The tripod is then placed on the phantom and the burr-hole guide moved into position such that the tip of the pointing rod is located in the centre of the ring which replicates the burr-hole.

The correct trajectory can now be set on the tripod and the depth stop clamp applied to the biopsy needle to determine the depth. If one is using a Sedan-type guillotine biopsy needle, at this point it is useful to firmly apply a 10m1 syringe to the proximal end needle and ensure that the inner cannula rotates easily when the syringe is rotated; the inner cannula is rotated such that

the biopsy window is closed prior to insertion. In order to ensure that the biopsy is taken from the chosen target, the depth stop is moved 5-7 mm proximally so that the target lies at the centre of the biopsy window.

The dura is now incised and the pia gently coagulated. The surgeon couples the tripod to the halo and this is securely held in place by the assistant. The biopsy needle is steadily advanced through the trajectory guide to the required depth with the outer window facing in the most appropriate direction. Often a definite resistance is felt as the tumour is encountered; the inner cannula is rotated until the windows are aligned and 4-5 ml of suction is applied to the syringe for a few seconds prior to closing the window by rotating the inner cannula. The inner cannula is then withdrawn, leaving the outer cannula in place while the assistant takes great care to avoid any movement of the tripod/halo complex.

The biopsy specimen is retrieved and placed on a glass slide- visual inspection should give an indication whether grossly abnormal tissue has been obtained. Further biopsies may be taken, rotating the outer cannula to sample in different directions. Biopsies may be taken either deeper or more superficially by making small adjustments in the position of the depth stop, and biopsies may also be taken from a different selected target by re-setting the tripod.

If clearly abnormal tissue has been obtained, it is not usually necessary to await intra-operative histological confirmation, but if there is any doubt it is prudent to wait until a provisional diagnosis has been made. The wound is closed in the usual fashion following which the halo is removed. Postoperatively the patient should ideally be admitted to the Intensive Care Unit, or at least High Care for observation for at least 6 hours. As the halo is re-usable, the recommended practice is to clean and then gas-sterilize it after each case so that it is sterile the next time it is used.

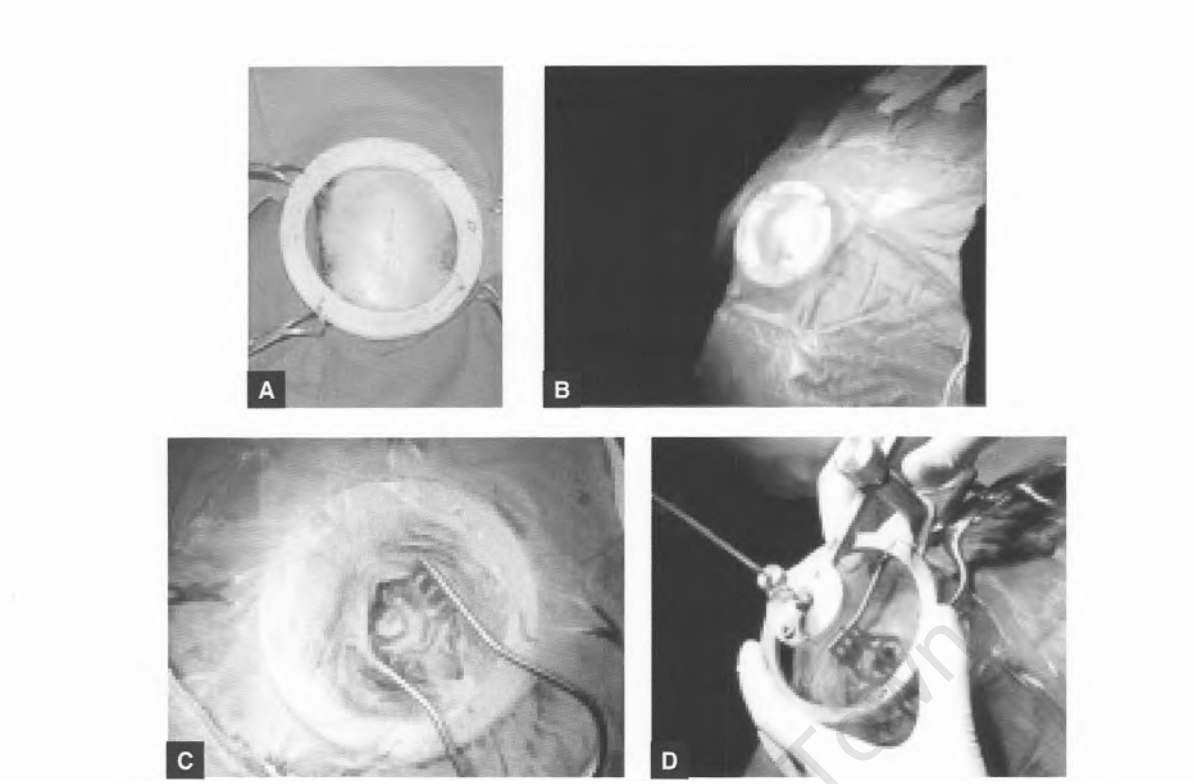


Figure A7: Surgery using the CTSP. The drapes should be secured circumferentially outside the halo, taking care not to exert traction on the scalp (a) following which an adhesive plastic drape may help to stabilize the halo (b). The burr hole is ideally placed in the centre of the halo (c) and the surgical procedure performed while an assistant stabilizes the tripod (d) (Picture credit: Mr PJ Mundell).

Appendix IV

Publications, presentations and awards related to this work

Publications

Peter JC, Fieggen AG, van Geems BA, Wynchank S, Adams LP (1995)
The Cape Town Stereotactic Pointer- a cost-effective stereotactic system.
Child's Nery Syst 11: 540 - 541

Adams LP, van Geems BA, Jaros GG, Peters J, Wynchank S (1995)
Stereophotogrammetric-controlled pointing device for neurosurgical use.
Med Biol Eng Comp 33: 212 - 217

Fieggen G, Taylor A, van Geems BA, Adams LP, Peter JC (1996)
The Cape Town Stereotactic Pointer; a novel neurosurgical system
S Afr Neurology Review, May:66

Adams LP, Peter JC, Fieggen AG, Taylor AG, Wynchank S, Adams LP (1998)
The Cape Town Stereotactic Pointer- a novel application of photogrammetry without cameras.
Photogrammetric Record 16 (92): 259 - 270

Taylor AG, Fieggen AG, Peter JC (1995)
Neuronavigation: Destination unknown.
S Afr Med J 89: 1171 — 1175.

Adams LP, Peter JC, Taylor AG, Fieggen AG, Wynchank S, van Geems BA (1999)
The Cape Town Stereotactic Pointer- a "back to basics" instrument.
Survey Review 35: 41 - 55

In Preparation

Fieggen AG, Taylor AG, van Geems BA, Adams LP, Peter JC.
The Cape Town Stereotactic Pointer; clinical experience.

Fieggen AG, Taylor AG, Parkes JD, Delport SV, Wilson JAG, Figaji AA, Peter JC.
Intra-tumoural bleomycin in cystic craniopharyngioma of childhood.

Presentations

Fieggen AG, Peter JC, van Geems BA, Wynchank S, Adams LP.

The Cape Town Stereotactic Pointer - a cost-effective stereotactic system.

XXIII Annual Meeting of the International Society for Paediatric Neurosurgery

Santiago, Chile. September 1995.

Fieggen AG, Taylor AG, van Geems BA, Adams LP, Peter JC.

The Cape Town Stereotactic Pointer.

14th Biennial Congress of the South African Neurosurgical Society

Durban, South Africa. May 1996.

Taylor AG, Fieggen AG, van Geems BA, Adams LP, Peter JC.

The Cape Town Stereotactic Pointer.

Computer Integrated Surgery

Linz, Austria. September 1997

Fieggen AG, Taylor AG, van Geems BA, Adams LP, Peter JC.

The CTSP: Towards stereotaxis for all.

Inaugural Meeting of the Indian Society for Stereotactic and Functional Neurosurgery

New Delhi, India. December 1997

Taylor AG, Fieggen AG, van Geems BA, Adams LP, Peter JC

The Cape Town Stereotactic Pointer.

2nd Arctic Stereotactic Conference

Baffin Island, Canada. July 1998

Fieggen AG, Taylor AG, Peter JC

Stereotactic Surgery using the CTSP.

8th Annual Meeting of the Indian Society for Stereotactic and Functional Neurosurgery

Bangalore, India. September 2004

Fieggen AG, Taylor AG, van Geems BA, Adams LP, Peter JC

Stereotactic approaches in children.

Society of Indian Paediatric Neurosurgeons- Neuropedicon

Chennai, India. October 2004

Fieggen AG, Taylor AG, van Geems BA, Adams LP, Peter JC

Development of the Cape Town Stereotactic Pointer.

13'" World Congress of Neurosurgery

Marrakech, Morocco. June 2005

Fieggen AG, Taylor AG, van Geems BA, Adams LP, Peter JC

Development of a simple frame-based stereotactic system: experience in children.

XXXIII Annual Meeting of the International Society for Pediatric Neurosurgery

Vancouver, Canada. September 2005

Fieggen AG, Taylor AG, van Geems BA, Adams LP, Peter JC

The development of the Cape Town Stereotactic Pointer.

18t" Biennial Congress of the South African Neurosurgical Society

Cape Town, South Africa. September 2006

Fieggen AG, Taylor AG, Figaji AA, Peter JC

Stereotaxis in Pediatric Brain Tumours.

World Federation of Neurosurgical Societies 13th Interim Meeting

Nagoya, Japan. November 2007

Hands-on Workshops

8th Annual Meeting of the Indian Society for Stereotactic and Functional Neurosurgery

Bangalore, India. September 2004

XX Congresso Colombiano

Cartagena, Colombia. November 2005

Presentations by others

Qureshi MM

Stereotactic procedures at the Agha Khan Hospital, Nairobi, Kenya.

10'" Asian Australasian Congress of Neurological Surgery

Lahore, Pakistan. November 1999

Devaprasad D, Andrew MA

Using the CTSP in the diagnosis of glioma.

8th Stereocon

Bangalore, India. September 2004

Gurunathan J, Sundarajan P

The Cape Town Stereotactic Pointer – our experience.

8th Stereocon

Bangalore, India. September 2004

Mohan NVS, Sridhar K

The Cape Town Stereotactic Pointer – an affordable alternative.

3rd South Asian Neurological Congress

Karachi, Pakistan. March 2005

Dugani S

The competitive advantage of the CTSP stereotactic system

10th Stereocon

Hyderabad, India. November 2006

Vekhende D

The Cape Town Stereotactic Pointer – a cost effective system

57th Neurocon.

Pune, India. December 2008

Qureshi MM

Stereotactic biopsy with the CTSP in HIV

1St African Federation of Neurological Surgeons Congress

Sharm El-Sheikh, Egypt. February 2009

Patents

RSA Patent No 94/1132

PCT Patent No PCT/NL95100063

SABS award

1997

South African Bureau of Standards/ Design Institute Award for Good Engineering Design

CE Mark

Awarded a CE mark in February 2002 as the CTSP was found to conform to the relevant provisions of EC Council Directive 93 / 42 / EEC

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