The clinical use and indications for head computed tomography scans in paediatric ambulatory care (short stay ward and medical emergencies) at a children's hospital over a one-year period, 1st January-31st December 2013

By

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DECLARATION

I, Dr Pamela Rudo Machingaidze, hereby declare that the work on which this dissertation/thesis entitled **The clinical use and indications for head computed tomography scans in paediatric ambulatory care (short stay ward and medical emergencies) at a children's hospital over a one-year period, 1st January-31st December 2013** is based on 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.

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List of Abbreviations

CT: Computed tomography

CSF: Cerebrospinal fluid

ED: Emergency department

HIV: Human Immunodeficiency Virus

LP: Lumbar puncture

MEU: Medical Emergency Unit

MRI: Magnetic Resonance Imaging

PACS: Picture Archiving and Communication System

RCWMCH: Red Cross War Memorial Children's Hospital

SSW: Short Stay Ward

UCT: University of Cape Town

VPS: Ventriculoperitoneal shunt

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1.1 Introduction

Computed tomography (CT) scanning is a vital diagnostic tool and plays a fundamental role in the diagnostic evaluation of paediatric intracranial pathology. It is important to ascertain why this investigative modality is being used in the South African paediatric emergency setting and whether judicious use is being made of this mode of investigation. Because of the structural detail that it provides which is inaccessible to the naked eye, it is considered essential neuroimaging. Despite this, in low and middle-income settings such as South Africa it is only accessible at secondary and tertiary level institutions, making its access inequitable. However, wherever it is used, from a good clinical practice stance, the onus is upon the clinician to use judicious clinical justification for each order of a CT scan. Numerous institutions across the globe have documented their experiences in the patterns of its use and possible concerns arising from that.

1.2 Aim of the literature review

The aim of this literature review was to summarise key issues relating to the clinical indications for performing head CT scans in children in the setting of emergency care, and to evaluate the results relating specifically to the immediate management of the patient along the pathway of care.

There is a large pool of published literature on head CT. This review focuses on the most frequent indications for head CT in children presenting with acute neurological illness as well as studies on risks associated with CT radiation. As many publications exist, in this study specifically, some of the frequently occurring indications for head computed tomography were identified and broad topics constructed to coordinate the search for relevant literature. The particular headings were constructed because a high burden of disease is concentrated around those acute neurological

presentations and many head CTs are ordered on their account. CT scanning, as an important diagnostic medical tool, contributes the major radiation exposure risk of all medical interventions. Also mentioned in this literature review is the discussion regarding the risks associated with radiation exposure and the work done to try to extrapolate, and hence quantify, the excessive cancer risks that some studies have highlighted [1-6].

1.3 Methodology of literature review

A structured non-systematic literature search was performed using MEDLINE via Pubmed (http://www.ncbi.nlm.nih.gov/pubmed). The search was limited to English language studies involving human participants between birth and 18 years of age.

A literature search performed on 31 October 2016 was conducted using the terms 'child*' OR 'children' (MeSH) AND 'CT' OR 'computed tomography' AND 'emergency' AND 'medical'; 'X ray computed tomography' OR 'CT scan' OR 'CT imaging' OR 'CAT scan' (MeSH) AND 'Head' AND 'paediatric' OR 'pediatric' OR 'child'. Five thousand four hundred and thirty-eight articles were retrieved.

The 5438 papers above were further screened for relevance using the search strings below together with titles and abstracts, with the resulting number of articles in parentheses:

- 'meningitis' (133 papers)
- 'Ventriculoperitoneal Shunt' OR 'VP shunt' OR 'Hydrocephalus' OR 'Hydrocephaly' OR 'Cerebral Ventriculomegaly' (MeSH) (319 articles)
- 'Seizures' OR 'convulsions' OR 'epilepsy' (MeSH) (244 articles)

- ‘Intracranial pressure’ refined with ‘increased’ OR ‘elevated’ OR ‘raised’ (MeSH) (112 articles)
- ‘Level of consciousness’ refined by ‘altered’ OR ‘depressed’ OR ‘decreased’ OR ‘impairment’ (14 articles)
- ‘Macrocephaly’ OR ‘megalencephaly’ (MeSH) (33 articles)

Papers that discussed the use of head CT investigation in trauma settings were excluded as the current study focused on medical emergencies.

More articles were identified by ‘snowballing’ from the references of articles initially found on the MEDLINE search. Alerts were also set up to email new relevant articles as they appeared on the database. Titles and abstracts were used to select relevant articles. The final screening yielded 35 articles which were included for review. These articles discussed the modality of CT investigation in medical scenarios, particularly involving medical emergency settings in which CT was indicated for suspected meningitis, suspected cerebrospinal fluid shunt pathology and seizures, as well as the concern over the exposure of paediatric patients to ionising radiation and possible long-term sequelae. Twenty-nine studies reported on the paediatric population; six reported on both children and adults. Two articles were from Africa, one from India, one from Thailand and 31 were from developed countries. Various articles were reviewed (Table 1).

Table 1: Articles included in the literature review on paediatric head CT usage

Article type	Number of articles
Retrospective review of case notes	7
Retrospective cohort	6
Prospective cohort	6
Prospective longitudinal cohort	1
Retrospective longitudinal cohort	1
Review article	4
Consensus guideline	3
Randomized controlled trials	2
Case series	1
Systematic review	1
Commentary	1
Letters to the Editor	2

CT – computed tomography

1.4 Results

The review that follows is organised under four key headings as these clinical scenarios represent the most common dilemmas facing clinicians within our practice:

1. Head Computed Tomography (CT) in patients with suspected meningitis
2. Head CT in patients with cerebrospinal fluid (CSF) shunts
3. Head CT in patients presenting with seizures
4. Risks associated with radiation exposure during head CT scanning

1.4.1 Head Computed Tomography (CT) in patients with suspected meningitis

A proportion of patients presenting with clinical features of meningitis undergo head CT scanning to assess whether it is safe to perform lumbar puncture (LP) on them. LP definitively diagnoses or rules out meningitis; however clinicians are often concerned about the possibility of precipitating cerebral

herniation (coning) if the patient has raised intracranial pressure, possibly resulting in death of the patient. Adhering to the Hippocratic principle that first we should do no harm, two questions arise in this matter:

1. What is the frequency of coning post lumbar puncture in patients with meningitis?
2. Is it possible to confirm the safety of LP on CT with absolute certainty?

An Australian study by Rennick et al., looked at children with bacterial meningitis [7]. The objective was to assess whether the incidence of cerebral herniation increases immediately after lumbar puncture and to look at head CT findings in children with herniation. The study was conducted at a large paediatric teaching hospital. Of the 445 children assessed, 19 (4.3%) had cerebral herniation. In two of the children herniation occurred twice, giving a total of 21 episodes. Thirty-one (7%) children died, of whom 14 (45%) had herniation. Of the 17 children who had a LP, 19 episodes of herniation occurred, 12 of which occurred in the first 12 hours post LP, and seven episodes over six other 12-hour periods. CT results were normal in five (36%) of the 14 herniation episodes. The study does not explicitly state whether cerebrospinal fluid (CSF) opening pressures were measured or not. They concluded that there was a strong suggestion that LP may cause herniation, and normal CT results do not mean it is safe to perform a lumbar puncture in a paediatric patient with bacterial meningitis [7]. The limitations of this study were that herniation was confirmed in only five children at autopsy, eight other children who died did not have autopsy done. There remains ongoing debate regarding whether LP causes herniation, leading to conflicting recommendation regarding timing of LP in children with suspected meningitis and reduced level of consciousness, and various recommendations regarding performing head CT prior to LP. Acute meningitis may result in cerebral swelling and fatal herniation even without lumbar puncture [7]. There may be clinically significant increased ICP without any abnormality on a CT scan. Indications for delaying LP in the above study included Glasgow Coma Scale <8, unresponsiveness to pain, focal neurological signs and decorticate or decerebrate posturing. It is crucial to establish clinically whether it is safe to perform the LP; clinical contraindications must not be ignored based on a normal CT result.

In a prospective study Cabral et al., looked at acute bacterial meningitis in 41 infants and children above the age of two months [8]. Serial CT imaging was performed at admission, discharge, and six to 18 months after treatment for bacterial meningitis. The authors established that clinical management was not influenced by CT findings, which did not show any clinically significant abnormalities that were not already suspected on clinical examination. For instance, all six (14.6%) patients with either focal infarction or pus in the basal cisterns had hemiparesis. Also, no focal parenchymal pathology was observed on CT scan without noting clinical neurological abnormality [8].

In 2013, a team of practitioners comprising the Federation of Infectious Diseases Societies of Southern Africa Working Group on Acute Meningitis in Children and Adults published consensus guidelines based on expert opinion for the management of acute meningitis in children and adults in South Africa [9]. They listed neurological contraindications to lumbar puncture without prior head CT scan as follows:

- Coma or markedly reduced conscious level (Glasgow Coma Scale <10)
- Papilloedema
- New unexplained focal neurological abnormality, for example hemiparesis or dysphasia
- Seizures with no apparent explanation
- Presence of cerebrospinal fluid shunt
- Caution was advised for patients with a combination of isolated cranial nerve palsies and reduced level of consciousness; the nerve palsies on their own were not deemed to be a contraindication.

Contraindications to LP after head CT are radiological features of gross generalised cerebral oedema or mass lesion with significant hemispheral shift [9].

1.4.2 Head CT and patients with cerebrospinal fluid (CSF) shunts

Cerebrospinal fluid shunts used in the treatment of hydrocephalus (HCP) comprise ventriculoperitoneal, ventriculopleural, ventriculoatrial, temporary external ventricular drainage and third ventriculostomy. Ventriculoperitoneal shunts, which are the commonest, are prone to numerous complications such as mechanical obstruction, malfunction, fracture, infection, migration and excessive CSF drainage [10]. A retrospective study in Louisiana in the United States analysed the long-term outcomes of ventriculoperitoneal shunt (VPS) surgery in 1015 patients with HCP, with the primary outcome of interest being shunt failure, whether revision or replacement after shunt insertion [11]. Eight had VPS surgery performed in the 1960s, 20 in the 1970s, 52 in the 1980s and 935 between 1990 and 2010. Two hundred and forty (78.2%) of the 305 paediatric patients required shunt revision versus 32.5% in the adult population ($p<0.01$). Single shunt revision occurred in 21.3% of paediatric and 19.7% of adult patients. Multiple shunt revision occurred in 57.4% of paediatric and 12.7% of adult patients. The mean number of shunt revisions in children was 2.6 (range 0–17) and 0.6 (range 0–11) for adults. Patients with history of previous shunt surgery had significantly greater shunt revision rates than those without previous shunt surgery (81.4% vs. 39.1%, $P < 0.01$). Statistically the odds for shunt revision in patients with prior shunt surgery were nine times higher than those without. Children were 4.22 times more likely to experience shunt revision [11]. A high index of suspicion for these complications should be maintained for children with VPS presenting to emergency departments (ED), as delay in rectifying problems may lead to severe morbidity, or worse still, mortality.

In a prospective multicentre cohort study commissioned by the Hydrocephalus Clinical Research Network, risk factors for shunt malfunction in 1036 children below 19 years of age with first-time shunt insertion were assessed [12]. In the cohort, 344 patients experienced shunt failure, demonstrating a failure rate of 33.2%. This represents one third of the patients which is a high

failure rate. A failure rate higher than 40% was reported in the second year following surgery in children who underwent shunt insertion before six months of age [12].

Most patients will be scanned frequently in their lifetimes. However:

1. Is it necessary for them to be scanned so often?
2. Are there distinguishing clinical features that make it imperative to scan some patients, while others become less urgent?
3. Can any adjustments be made to the radiation dose to reduce the cumulative effect?

Two multicentre prospective randomized controlled trials in Michigan focused on diagnosing failure of VPS clinically [10]. Bulging fontanelle, collection of fluid around the shunt, depressed conscious level, irritability, abdominal pain, nausea and vomiting, accelerated cranial growth and headache were strongly associated with shunt failure. Fever, gross signs of wound infection, drainage of pus, meningism, peritonitis and CSF leakage were associated with shunt infection. Irritability was identified as an important observation for both shunt failure and infection. Loss of upgaze eye movement was also highly significant [10]. Picking up highly suggestive clinical features and referring those patients for CT scan versus the current practice of performing head CT on every child with a VPS presenting to the emergency department (ED) could help to curtail unnecessary exposure of patients to frequent irradiation.

A multicentre study also done in the US looked at 1319 children with ventricular shunts seen across 31 hospitals, with a total of 6636 ED visits over a 10-year period [13]. Almost half (49.4%) of all ED visits culminated in a head CT, and about 6% of patients received 10 or more scans, accounting for just over a third (37.2%) of all ED visits with a CT, indicating that a small proportion of children were scanned the most. Twenty percent of the visits where CT was obtained required revision of the shunt. Notably, many children who didn't require operative intervention received multiple scans. Regarding scanning frequency, this was highest within the two years following initial shunt

placement, when risk for revision as well as vulnerability to ionizing radiation are highest. The last two observations may be attributed to the fact that it is challenging to distinguish clinically between shunt malfunction and other common clinical syndromes in young children, as symptoms like vomiting or headache can also indicate gastroenteritis or migraine. The authors noted significant variability across the hospitals in performing CT scan for VPS evaluation, and postulated that there is a paucity of strong evidence to guide clinical decision-making, further complicated by medico-legal concerns and institutional culture. They recommended that further research is required to identify patients with a higher risk for shunt malfunction using clinical prediction tools [13]. The fact remains: if a malfunctioning shunt is not appropriately identified and diagnosed, whether clinically or radiologically, the child will cone and either die or suffer severe irreversible neurological damage.

1.4.3 Head CT and patients presenting with seizures

First onset seizures, focal seizures, complex febrile seizures and breakthrough seizures are commonly used by clinicians as indications for head CT scanning.

In 2007 the American Academy of Neurology, through its Therapeutics and Technology Assessment Subcommittee, published an evidence-based systematic review on neuroimaging in the emergency patient presenting with seizure in both adults and children [14]. The objective was to reassess the value of neuroimaging as a screening procedure for providing information with a bearing on acute management, as well as to assess clinical features associated with abnormal imaging results. Fifteen articles were reviewed. The conclusions were that CT in the ED for children with first-onset seizures will change acute management in approximately 3-8%, with no clear difference between rates of abnormal emergent CT for patients with chronic seizures compared to first-onset. CT abnormalities resulting in change in emergency management were cerebral haemorrhage, neoplasms, neurocysticercosis and obstructive hydrocephalus. Fifty per cent of the time, children presenting

with seizures below 6 months of age have a high incidence of clinically significant abnormalities on CT. Focal abnormalities on neurological examination, predisposing history or focal seizure onset are likely predictive of abnormal CT results. The following recommendations were made:

- An emergency CT may be considered in children with first onset seizure
- Emergency CT is not recommended for patients with chronic seizures
- Consider emergency CT in children under 6 months of age presenting with first onset seizures [14].

A prospective cohort study at Red Cross War Memorial Children's Hospital (RCWMCH) investigated the diagnostic yield of head CT in paediatric patients presenting with first-onset partial seizures in an area with a high prevalence of neurocysticercosis and tuberculosis (TB) [15]. One hundred and eighteen children ranging in age from six months to 12 years were enrolled. There was no age-based stratification. Ninety-five children had CT scans, and the remainder were lost to follow-up; 94 (79.7%) CT results were available which were subsequently analysed. The median age of the patients was 94 months (IQR 33-99). In 32 children (34%) the scans were reported as being normal, 45 (48%) exhibited single or multiple granulomas, and 17 (18%) demonstrated other findings. Five scans (5%) showed incidental findings of no clinical significance, and four (4%) showed findings of uncertain significance, of whom those patients were discharged after follow-up. Eight (8%) patients had specific findings that were suspected before the CT scan. None of the patients had meaningfully abnormal CT findings besides neurocysticercosis that were not already clinically suspected prior to CT. Researchers concluded that routine CT imaging did not meaningfully alter clinical management of the 94 children. The authors extrapolated that 26 CT scans would be required to detect one unsuspected abnormality that would be clinically meaningful besides neurocysticercosis. They also extrapolated that, assuming that albendazole reduces the risk of subsequent seizures from 33% to 13% based on a statistical estimate of its effect [16], routine CT imaging would require 11 scans and

5 courses of albendazole to prevent one more paediatric patient from experiencing seizures, compared with no CT imaging and 11 courses of albendazole with blanket albendazole use [15].

At Schneider Children's Hospital in New York, a team studied the role of brain CT in evaluating children with new onset seizures in the ED [17]. A year-long retrospective review of case notes of all paediatric patients presenting with first-onset seizures to the ED who underwent brain CT was performed. Patients with simple febrile seizures were excluded. Of the 66 patients, 14 (21.2%) had abnormal results. The cause of seizures was deemed unknown in 33 patients, two of whom had abnormal results but neither warranted intervention. In 20 patients, 12 of whom had abnormal results, the cause was considered symptomatic. Two of the patients with abnormal results had findings of therapeutic significance which were foreseen from prior clinical evaluation. Of 13 patients with complex febrile seizures, none had an abnormal scan. Patients with partial seizures were more likely to have abnormal scans compared to those with generalised seizures, although the difference was not statistically significant. The authors concluded that routine brain CT scans for all patients with new onset non-febrile seizures is not justified, and history and examination are enough to pick up patients warranting imaging. Emergency CT imaging is not indicated for patients without known seizure risk factors, with normal neurological examination, and no acute symptomatic cause besides fever. Rather referral to a paediatric neurologist for evaluation including electroencephalogram (EEG) and more appropriately magnetic resonance imaging (MRI) would be more suitable [17].

In West Virginia, Allen and Jones looked at 21 children with epilepsy presenting with breakthrough seizures and undergoing head CT scanning [18]. None of the scans had acute findings and they were all discharged from the emergency department, suggesting that the yield of emergent CT scans in epileptic children with breakthrough seizures is low [18]. This corresponds with the recommendation

by the American Academy of Neurology stating that emergency CT is not useful for patients with chronic seizure conditions [14].

Physicians in Atlanta conducted a retrospective review of case notes to determine the clinical factors associated with a more extensive workup in children presenting with complex febrile seizures, defined as febrile seizures with a duration of 15 minutes or more, more than one seizure in a 24-hour period, and/or focal in nature. The investigators found that, of the 199 patients enrolled, 53 (28%) had a head CT performed, and no significant findings to assist with management were noted; further, patients presenting with focal seizures and patients who received anticonvulsants either in the emergency department or en route to hospital had greater odds of getting a head CT. The latter presented with altered mental state making their clinical assessment challenging. Practice guidelines are necessary for evaluation of these patients to reduce the amount of imaging [19].

Certain clinical features can often be predictors of abnormal CT findings. Warden et al., in Seattle set out to develop guidelines for clinical decision-making using clinical features of paediatric patients presenting to the ED with seizures, in order to predict abnormal CT results [20]. In a sample of 203 patients with a median age of 3.1 (IQR 1.1-6.1) years, analysis revealed that normal CT results were associated with patients who had no pre-existing high-risk condition such as malignancy, neurocutaneous syndrome, closed head injury or CSF shunt revision in the preceding 6 weeks, were above the age of six months, had fitted for 15 minutes or less, and had no history of new onset focal neurology. A retrospective application of those criteria would have deferred 41% of the CT scans performed. Notably this study also included trauma patients, who were excluded from our study [20].

In Thailand, Sanmaneechai et al., identified characteristics in epileptic children aged one month to two years that are predictive of abnormal neuroimaging findings. Half the children had CT only, 14 (38%) had MRI, and 4 (11%) had both CT and MRI. They found that the younger the age, the higher the chances of abnormal imaging results; other predictors were developmental delay, abnormal head circumference and abnormal findings on neurologic examination [21]. The young age may be attributable to the vulnerability of the very young brain, which undergoes maximal growth and development prenatally extending into the first year of life; abnormalities in structure or dynamic organisation occurring during this delicate time may influence major clinical manifestations early on in life.

1.4.4 Risks associated with radiation exposure

CT examination exposes patients to high doses of radiation. In adults, the radiation dose in a single abdominal CT scan is equivalent to 500 chest radiographs [22]. The dose in a single head CT is equivalent to 100 chest radiographs [23]. In children, the following factors further compound the risk:

- Children, being more radiosensitive, are 10 to 15 times more likely to develop malignancy than an adult after exposure to the same radiation dose
- Proximity of other tissues and organs, for example the thyroid gland, to the cranial CT imaging site results in greater radiation exposure
- The rapid turnaround time in which CT is performed with little or no sedative needed makes it tempting to use as a screening procedure [24].

There has been growing concern over cancer risks from radiation exposure in paediatric CT, considering the rapidly increasing frequency of imaging with CT in children. There is data to suggest that brain tissue is far more radiosensitive than previously thought. Age at exposure seems to modify the risk, with it being higher in individuals exposed early in life. [25]. In rare circumstances of

prolonged, high-dose ionising radiation exposure, other adverse health effects, such as skin erythema, tissue injury, and birth defects following in-utero exposure can occur [26].

Due to multiple episodes of imaging, patients with CSF shunts are exposed to more episodes of radiation which possibly lead to an increased excessive risk of malignancy. Smyth et al., documented two cases where it is thought to be likely that excessive radiation exposure contributed to the development of head and neck malignancies [27]. One patient was 18 years old, with a VPS from three weeks of life. He underwent a total of 23 head CT scans and 25 skull radiographs and required 23 VPS revisions in his lifetime. At age 17 years he developed Hodgkin's lymphoma in the cervical region of his shunt tract, for which he was treated successfully. The second patient received a shunt at two months of age, underwent 13 VPS and ventriculoatrial shunt revisions and had 14 head CT scans before he was 15 years old. At age 19 he was diagnosed with a gliosarcoma to which he succumbed despite aggressive therapy. However, the article did note that causation cannot be established with certainty due to multiple factors involved in the scanning episodes [27]. Aldrink et al., also documented a cohort of 112 patients with shunted hydrocephalus, of whom 13.6% developed thyroid nodules detected on ultrasonography. No malignancies were detected. The mean age of the enrolled patients was 19 years (SD +/-8.1 years) and number of head CT scans was 23 (SD +/-14) per patient. The patients in whom nodules were detected were older (mean age 24.3 ± 7.6 years versus mean age 18.4 ± 8.0 years for those without nodules; p=0.005), with a longer follow-up time compared to those without nodules, illustrating that time of exposure to radiation is significant. They concluded that during diagnostic imaging of the head and neck these patients are exposed to substantial amounts of radiation predisposing them to development of thyroid nodules and possibly malignancy and recommended ongoing surveillance [28].

Efforts have been made to estimate radiation doses and extrapolate lifetime cancer risks. A study conducted by radiologists in New York postulated that in the US, of about 600 000 abdominal and head CT examinations performed annually in children below the age of 15 years, roughly 500 might ultimately die from cancer attributable to the CT radiation [2].

In Israel, Chodick et al., set out to estimate the number of excess lifetime malignancy-related deaths associated with annual CT scans performed in children [4]. Over a 5-year period they looked at gender and age-specific CT scan use nationwide. Based on published organ doses for common CT examinations and radiation-related malignancy mortality risk estimates from studies in survivors of the atomic bomb, excess lifetime risks for malignancy mortality due to CT utilisation in children and adolescents were estimated. The authors estimated that 17 686 scans were performed on children annually during the years 1999-2003, and projected that 9.5 lifetime deaths would be associated with one year of CT scanning in children below 18 years of age and about 7.25 for those scanned below 15 years of age, representing an excess of 0.29% over the total number of patients eventually estimated to die from a malignancy in their lifetime. They concluded that this excess lifetime risk is small, but not negligible, and that all health workers involved should endeavour to minimise the radiation dose for children and encourage judicious use of CT as it is an indispensable diagnostic tool [4].

In France, Journy et al., gave predictions of potential lifetime cancer risks induced by childhood CT examinations using routine practices. They estimated organ doses from standard protocols in 15 hospitals. Excess risks of leukaemia, central nervous system (CNS), breast and thyroid cancers were predicted from estimates in the Japanese atomic bomb survivors' cohort and medical exposure studies. They predicted that 100 000 head CT scans in five-year-old children would result in eight CNS cancers and four cases of leukaemia; 100 000 chest scans would lead to 31 thyroid cancers, 55

366 breast cancers and one case of leukaemia. Lifelong risks would be low for individuals, but relative
367 risks would be highest in the first decades of life [5].

368

369 In the United Kingdom another study attempted to project the risks of developing malignancy, and
370 to estimate cases potentially induced by past, current and future CT performed in patients under 20
371 years of age. The 130 750 scans of 2015 were projected to induce 64 cancers in the future. Current
372 practices would result in about 300 future cancers induced by scans performed in 2016-2020 [6].

373

374 In light of the above, there has been a movement towards the use of imaging settings with a lower
375 radiation dose, the concept of ALARA (As Low As Reasonably Achievable). This concept endeavours
376 to use the lowest possible radiation dose without compromising the diagnostic quality of images. In
377 2001 the Society for Paediatric Radiology convened a multidisciplinary conference in the United
378 States to clarify issues regarding paediatric CT. They acknowledged the existing evidence of the
379 excess cancer risk associated with radiation exposure, as extrapolated from atom bomb survivors
380 whose radiation exposure is comparable to the dose received in helical CT. The risk is small but was
381 deemed to be statistically significant. The panel also reiterated that radiosensitivity in children is 10
382 times that in adults. They emphasised that by no means should the dose be reduced such that
383 imaging quality is compromised hence rendering the examination useless, but emphasis should be
384 avoiding CT use where it is not needed, for example as a screening procedure. The consensus was
385 that radiation doses need to be modified to the lowest effective dose for children, and robust
386 indications should be present for doing the investigation [29]. As a result of this conference an FDA
387 public health notification was released to radiologists, radiation health professionals, risk managers
388 and hospital administrators regarding the reduction of radiation risk from CT for paediatric and small
389 adult patients. The recommendations were, in summary:

1. Optimize CT settings by tube current reduction, using charts of tube current settings based on patient weight or diameter and anatomical region of interest, and increasing table increment (axial scanning) or pitch (helical scanning)
2. Cut down the number of multiple scans using contrast
3. Curtail inappropriate CT referrals [30].

A group of surgeons and radiologists in Oregon investigated the use of a modified head position, the 'exaggerated sniff', together with a commercially available iterative reconstruction CT technique as well as reduced radiation dose to perform paediatric craniofacial imaging. This head position with a fully extended neck removes the thymus and cervical structures including the thyroid gland (which are two very radiosensitive organs) from the field of view, reducing their exposure to radiation, and simultaneously includes the whole head. Previously the authors had shown an 18% effective radiation dose reduction using the modified head position alone, while maintaining the diagnostic quality of the images [31]. Their results with the combined modalities of head position and dose reduction showed a 56.7% reduction in the imaging-related effective radiation dose [32].

Regarding patients with VPS, limited slice protocols have been investigated for monitoring patients with VP shunts. A study in Pittsburg on both children and adults was conducted where neuroradiologists selected three slices from specific anatomical landmarks and reported findings from those CT images. They concluded that unenhanced head CT with limited 3-slice protocol gives adequate information for diagnosing of VPS malfunction with more than 90% reduction in effective dose. However, this limited protocol is only indicated specifically for the investigation of shunt malfunction. Missed findings were acknowledged but were not life-threatening or acute [33].

On the other hand, recently a community in paediatric radiology believe that excess risks of cancer attributable to CT radiation are miniscule, if at all they exist. They hold the opinion that evidence thus far indicating risk has not been overwhelming, and the belief is that many CT scans that are warranted and indicated are being denied unnecessarily, and the burden on anaesthetists and MRI lists is being unnecessarily added to [34, 35]. Cohen also expressed that the risk of cancer from CT is surpassed by the risk of an incorrect diagnosis emanating from not doing a CT scan. The concern is that there has been unnecessary media hype in articulating CT risks, causing alarm to parents who may not consent to CT imaging fearing that their children may develop cancer. Cohen, in response to Andronikou's article noted that the topic of cancers attributed to radiation has fuelled media articles that generate fear in the public, "despite the fact that CT radiation induced cancer remains an unproven hypothesis with no valid supporting evidence". He argued that campaigns like ALARA have caused confusion for referring physicians and have alarmed patients by indicating that there is a significant risk hence radiation doses should be reduced. He states that a clinically indicated CT scan will far exceed any risk, and encourages clinicians and radiologists to apply all the principles of 'excellent, correct imaging', providing holistic care to patients, beyond the focus of CT radiation and cancer [36].

1.5 Conclusion

In summary, the literature review has focused on addressing key elements that are faced in managing children presenting to emergency departments with neurological symptoms and signs. Whilst value in children with CSF shunts has been demonstrated there is little consensus on when head CT scans should be done in other clinical settings like suspected meningitis and seizures. The review has highlighted the value of brain CT scanning, but has also raised awareness of potential risks associated with exposure to ionizing radiation. Despite the opinion that the risks are possibly being overcalled, the consensus in the world of paediatric radiology is that exposure to radiation

through computed tomography scanning does pose a risk of developing malignancy in children, as they are particularly radiosensitive. As such, it is vital that appropriate indications for CT be applied with sound protocols, especially in a medical emergency setting.

The study that follows aims to explore the patterns of use of head CT scanning in the medical emergency department of a tertiary level paediatric hospital in South Africa over a 12-month period. The main areas of interest include indications for head CT scanning, excluding trauma, and the frequency of abnormal findings, with or without subsequent intervention, mainly of a surgical nature.

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Chapter 2: Publication-ready Manuscript

The clinical use and indications for head computed tomography scans in paediatric ambulatory care (short stay ward and medical emergencies) at a children's hospital over a one-year period, 1st January-31st December 2013

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Abstract

Background: Computed tomography (CT) imaging is an indispensable tool in the management of acute paediatric illness. It offers quick answers, allowing timely lifesaving decision-making. Clinical evidence is required to maximise its benefits against radiation-exposure risks to patients and cost to the healthcare system.

Aims: The study aimed to retrospectively investigate clinical presentation and indications of head CT at a tertiary paediatric hospital.

Methods: Records of children presenting with acute illness to the medical emergency unit, excluding trauma, of Red Cross War Memorial Children's Hospital, Cape Town, over one year (2013) were retrospectively reviewed. Participants were included if they underwent head CT scan within 24 hours of presentation. Clinical data were extracted from records and CT findings reported by a paediatric radiologist.

Results: Inclusion criteria were met by 311 patients; 188 (60.5%) were boys. The median age was 39.2 (IQR 12.6-84.0) months. Commonest indications were seizures (n=169;54.3%), reduced level of consciousness (n=140;45.0%), headache (n=74;23.8%) and suspected ventriculoperitoneal shunt (VPS) malfunction (n=61;19.7%). In 217 (69.8%) patients CT showed no adverse findings. In the 94 (30.2%) patients in whom CT abnormalities were detected, the predominant findings were hydrocephalus (n=54;57.4%) and cerebral oedema (n=29;30.9%). Abnormal CT findings were commoner in patients with nausea or vomiting (n=21;9.3%, p=0.05) papilloedema (n=3;1.3%, p=0.015) and long tract signs (n=23;10.2%, p=0.02). Forty-seven patients (15.1%) required surgical intervention after CT of which 40 (85.1%) needed a ventricular drainage procedure. A larger proportion of patients with VPS (25/62;40.3%) required surgical intervention compared to patients without VPS (22/249;8.8%, p<0.001).

Conclusion: Most children presenting with acute illness (excluding trauma) and undergoing emergency head CT have normal findings. Patients with ventriculoperitoneal shunts constituted a

large proportion of patients requiring intervention after CT. Considerations should be made to use clinical presentation to select patients most likely to benefit from CT.

Introduction

Computed tomography (CT) is an indispensable tool in the management of paediatric illness; particularly in the acute diagnosis of medical or surgical intracranial pathology. It can give answers quickly, allowing potentially lifesaving decisions to be made urgently [1-3].

A number of studies show that CT head or brain is the commonest CT examination in children [4-6]. This contrasts with older age groups in which abdominal and pelvic CT scans predominate [7, 8].

The benefits of CT must be weighed against the risks to the patient and health care system. CT carries potential risk of malignancy because of its associated ionizing radiation. This is particularly so in children who are more radiosensitive than adults, and can lead to leukaemia and brain tumours [9]. Using data sourced from atomic bomb survivors, one model estimated that for every 600 000 abdominal and head CT examinations performed in children under the age of 15 years, 500 will ultimately die from radiation attributable malignancy [10]. Other effects of high-dose ionising radiation exposure include skin erythema, tissue injury, and birth defects following in-utero exposure [11]. CT imaging also carries infrastructural costs associated with the need for sedation required to achieve optimal imaging results in children. Consequently, in addition to radiographer and radiologist time, anaesthetic staff is required to ensure safety of the airway and monitoring of breathing during the procedure.

There is need to have evidence-based guidelines for performing CT to minimize cumulative radiation doses and avert long-term sequelae. In high income countries, attempts have been made to create tools for estimating cumulative radiation exposure as well as calculating associated risks of malignancy [12].

There is some published data on the use of CT in Africa in the management of meningitis and paediatric seizures [13]. However, data are generally very limited to guide practice in resource limited settings on the use of CT in acute paediatric medical illness [14]. Our study aimed to investigate the clinical utility of emergency head CT scan investigations at a tertiary paediatric hospital in a low and middle-income country (LMIC) setting. The primary outcomes of interest were indications for and findings of head CT imaging in children presenting for acute medical care, as well as to establish baseline characteristics and interventions performed post CT scanning. Secondarily, we explored presenting factors that predict abnormal findings on CT. The null hypothesis postulated that most head CT scans done in children presenting acutely in the medical emergency department would demonstrate normal findings, or findings which would not be of acute clinical significance.

Methods

A retrospective observational study was done on a cohort of children presenting with acute medical illness requiring CT scan of the brain. A list of CT scans performed over one year was compiled from the radiology department's Picture Archiving and Communication System (PACS) of the Red Cross War Memorial Children's Hospital (RCWMCH), Cape Town, South Africa. RCWMCH is a tertiary referral hospital servicing a paediatric population of about 1.5 million children. All children seen in the medical emergency unit (MEU) from 1 January 2013 to 31 December 2013 who underwent brain CT imaging within 24 hours of consultation or admission were eligible for inclusion. Subjects were

excluded if referral for CT was not done in the MEU as part of their assessment; injured children are seen in a separate trauma unit at this institution. Demographic data were extracted from records, and indications for CT as well as clinical presentation were documented for each child. CT findings as independently reported by an experienced paediatric radiologist were noted.

Head CT scan findings were classified as normal (clinically insignificant) if a first-time scan was reported as normal or where no interval change on CT findings of a participant with known pre-existing abnormality on CT was found. CT findings reported as abnormal in first-time CTs or where interval change had occurred in subjects with known abnormal findings on previous CT were regarded as abnormal (clinically significant).

Data were analysed using STATA software version 13 (STATA Corporation, College Station, Texas, USA). Categorical variables were represented as proportions using percentages. Continuous variables were summarised using medians with interquartile ranges (IQR). Categorical variables were compared using Chi-square tests.

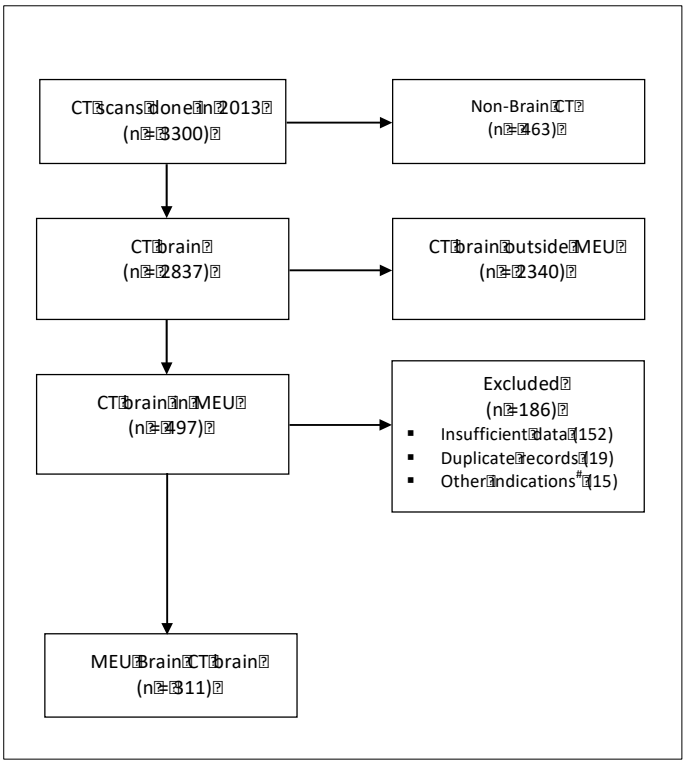
Approval for the study was granted by the Research Ethics Committee of the University of Cape Town, and the administration of RCWMCH; Ethics reference HREC/Ref: 087/2015.

Results

Baseline characteristics of included study subjects

A total of 311 subjects, representing 9.4% of the 3300 CT scans done in the hospital in 2013 met inclusion criteria (Figure 1). The cohort included 188 boys (60.5%). The median age of the group was 39.2 (IQR 12.6-84.0) months and ranged from two and a half weeks to 15 years of age. There were 62 (19.9%) patients who had cerebrospinal fluid (CSF) shunts, one of whom had a ventriculopleural shunt, three had cystoperitoneal shunts and the rest had indwelling ventriculoperitoneal shunts. None of the patients had endoscopic third ventriculostomy. In addition to having CSF shunts, 25 (40.3%) of shunted patients also had a diagnosis of epilepsy.

Figure 1: Flow diagram of sample selection for enrolment



#CT done for ophthalmology and otorhinolaryngology purposes

CT – computed tomography

MEU – medical emergency unit

For 225 (72.3%) of the study subjects this was their first head CT scan. In 74 (86.0%) out of 86 patients for whom the 2013 scan was a repeat, the number of previous scans could be determined. The median number of previous scans was four (IQR 2-7), ranging from one to 22 scans for a total of 365 previous scans. Individuals with CSF shunts accounted for 62 (72.1%) of patients with previous

head CTs and 322 (88.2%) of the total known number of previous scans. The total number of previous scans could not be ascertained for 12 of the patients. One child, a two-year-old female with hydrocephalus secondary to neonatal meningitis and a ventriculoperitoneal shunt (VPS) in situ, had the highest number of head CT scans. She was scanned 5 times during 2013 and 22 times in her lifetime. The same patient underwent three VPS revisions in 2013.

Table 1: Baseline characteristics of study participants

Baseline characteristic	***N=311***
Age	
Median IQR months	39.2 (12.6-84.0)
	n (%)
Gender	
Female	123 (39.5)
Male	188 (60.5)
Origin	
Referred	191 (61.4)
Self-referred	101 (32.5)
Unknown	19 (6.1)
First scan	225 (72.3)
Repeat scan	86 (27.7)
CSF shunt in situ	62 (19.9)
No CSF shunt in situ	249 (80.1)
Known epilepsy diagnosis	54 (17.4)
Previous seizures	30 (9.7)
HIV status	
Unexposed uninfected	158 (50.8)
Exposed uninfected	31 (10.0)
Infected	7 (2.2)
Unknown HIV status	115 (37.0)

IQR – interquartile range
CSF – cerebrospinal fluid
HIV – human immunodeficiency virus

Indications for head CT

Ninety-six (30.9%) decisions to perform CT were made by senior staff, that is, paediatric consultants and senior registrars. Most requests (n=163;52.4%) were made by junior staff, comprising junior paediatric and neurosurgical registrars, medical officers and interns. For the remaining 52 (16.7%) patients it could not be established from the patient record who had ordered the scan.

The median time from ordering the head CT to performing it was 63 (IQR 38-112) minutes, ranging from 10 minutes to 21.7 hours.

Indications for CT have been shown in table 2 in descending order of frequency. The majority of study subjects had more than one indication.

Table 2: Indications for head computed tomography in children presenting with acute medical illness to RCWMCH in 2013

Indication#	n (%)
Seizures	169 (54.3)
Impaired level of consciousness	140 (45.0)
Headache	74 (23.8)
Suspected VPS pathology	61 (19.7)
Focal neurological signs	42 (13.5)
Suspected raised intracranial pressure	26 (8.4)
Suspected hydrocephalus	23 (7.4)
Suspected tuberculous meningitis	8 (2.6)
Other	23 (7.4)

 # majority of study subjects had more than one indication
RCWMCH – Red Cross War Memorial Children's Hospital
VPS – ventriculoperitoneal shunt

The commonest indication for CT was seizures (n=169; 54.3%) with 63 (37.5 %) of the patients having generalised seizures, 59 (35.1%) focal and eight (4.8%) classified as atypical. In 28 (16.7%) both focal and generalised seizures co-existed while the type of seizure was unknown in 10 (6.0%). The median seizure duration was 15 (IQR 5-30) minutes, with the longest seizure lasting 4 hours (240 minutes) and the shortest less than a minute. In 49 (37.7%) of the participants, a diagnosis of status

epilepticus (SE) was made by the attending clinician, defined as a seizure lasting more than 30 minutes. The presenting seizure was the first seizure episode for 53 (31.4%) of the patients while 54 (17.4%) had a pre-existing diagnosis of epilepsy. The remaining 30 (9.7%) had experienced previous seizures, although no diagnosis of epilepsy was made. Of the patients who had prior head CT scans, 28 were known with a diagnosis of epilepsy. Twenty-eight (16.6%) patients were documented as having febrile seizures.

Findings on CT scan

In 169 (54.3%) patients the CT scan findings were normal, while 50 (16.1%) showed no change from previous CT findings, collectively giving 219 (70.4%) with no clinically significant findings on current CT. Fifty-six patients (18.0%) undergoing CT for the first time had abnormal findings on CT, while 36 (11.6%) had pathological interval change on known previous CT findings, adding up to 92 (29.6%) patients with significant abnormal CT findings on current scan.

Hydrocephalus was the commonest abnormal finding with 54 (58.7%) of the 92 abnormal CTs showing this finding. Twenty-nine patients with CSF shunts presented with hydrocephalus on CT scan. This was followed by cerebral oedema in 29 (31.5%). The other abnormal CT findings are shown in table 3.

Table 3: Findings on head computed tomography (CT) in 311 children presenting with acute medical illness

Finding on CT#	n (%)
Normal	219 (70.4)
Hydrocephalus	54 (17.4)
Cerebral oedema	29 (9.3)
Space occupying lesion	19 (6.1)
Cerebral atrophy	16 (5.1)

Meningitis*	12 (3.9)
Infarct	11 (3.5)
Surface collection	10 (3.2)
Haemorrhage	4 (1.3)
Thrombosis	3 (1.0)

 # some study subjects had more than one abnormal finding
***meningitis – basal meningeal enhancement, leptomeningeal enhancement, subdural hygroma**

Fifteen (27.8%) of the 54 patients with a known diagnosis of epilepsy had normal findings on CT while 21 (38.9%) had known pre-existing pathology which was unchanged. A total of 18 (33.3%) patients with epilepsy had abnormal CT findings of which six (33.3%) were findings on first time CT and 12 (66.7%) interval change on pre-existing CT pathology.

Frequency of abnormal or clinically significant findings was slightly higher though not significant in patients who presented without seizures compared to those with seizures with 49 (34.5%) out of 142 and 43 (25.4%) out of 169 respectively; P=0.081. Lack of association between presence of seizures and abnormal CT findings was noted irrespective of the type and duration of seizure (Table 4). In patients with seizures lasting more than 15 minutes, of the patients scanned for the first time, 38/86 (44.2%) had normal findings versus 10/24 (41.7%) with abnormal findings (p=0.826); of the patients receiving a repeat scan 10/15 (66.7%) had no interval change while 2/5 (40%) had new findings (p=0.292).

Table 4: Comparison of CT findings in patients with first and repeat CT by clinical presentation

Clinical Presentation	First Computed Tomography n(%)			Repeat Computed Tomography n(%)		
	Normal n=169	Abnormal n=56	P	No change n=50	New findings n =36	P
Impaired LOC	84 (49.7)	35 (62.5)	0.096	27 (54.0)	16 (44.4)	0.382
Nausea or vomiting	41 (24.3)	21 (37.5)	0.055	22 (44.0)	22 (61.1)	0.117
Papilloedema	0 (0.0)	3 (5.4)	**0.015**	1 (2.0)	3 (8.3)	0.304
Generalised seizure	61 (36.1)	16 (28.6)	0.304	9 (18.0)	5 (13.9)	0.610
Headache	28 (16.6)	11 (19.6)	0.598	18 (36.0)	17 (47.2)	0.296
Long tract signs[#]	42 (24.9)	23 (41.1)	**0.020**	15 (30.0)	11 (30.6)	0.956
Focal seizure	53 (31.4)	20 (35.7)	0.546	10 (20.0)	4 (11.1)	0.271
Focal neurology	18 (10.7)	8 (14.3)	0.461	10 (20.0)	6 (16.7)	0.695

LOC= level of consciousness; CT= computed tomography; Bold typeface=P<0.05; # Increased tone and brisk reflexes

Abnormal CT findings on current CT were found in 31 (50.0%) out of 62 patients with CSF shunts compared to 61 (24.5%) out of 249 in those without shunt; P<0.001.

Of the 169 patients with seizures, 151 (89.3%) did not have CSF shunts. In that cohort, 44/151 (29.1%) had abnormal findings on CT scan.

Management and outcome

One patient, a 17-month-old male, experienced a severe reaction to intravenous non-iodinated contrast. This manifested as desaturation accompanied by swelling of lips and eyelids. He received intravenous promethazine, to which he responded positively without residual morbidity.

A total of 160 LPs were performed on 158 patients (2 patients had LP before and after scan). Of this group, 21 (13.1%) LPs were performed before CT scan and 139 (86.9%) after CT scan. In 70 (50.4%) patients with suspected meningitis who had LP post CT scan, CT was done first to exclude space-occupying lesions, non-communicating hydrocephalus or raised intracranial pressure, contraindications for LP. Only two (2.9%) of these had radiological contraindications to LP. Both patients were previously well. One patient presented with fever, seizures, impaired level of consciousness, irritability, global hypotonia and ataxia. The CT showed brain swelling with effaced surface sulci and basal cisterns. The LP was deferred, and the patient treated empirically for meningitis. It was performed nine days later after a repeat CT done four days after the initial scan showed interval improvement. The cerebrospinal fluid (CSF) was clear and colourless, there were no polymorphonuclear (PMN) leucocytes, five lymphocytes and 105 erythrocytes. The Gram and Ziehl-Nielsen stains demonstrated no organisms and no growth was obtained on culture. The biochemistry was normal. The discharge diagnosis was ‘meningitis with seizures’. The second patient presented

with first-onset prolonged focal seizures with impaired level of consciousness, vomiting, fever and meningeal irritation. The CT showed diffuse brain swelling with effacement of sulci and basal cisterns. LP was deferred and empiric therapy for bacterial and tuberculous meningitis plus herpes encephalitis was commenced. Two days later the CT was repeated and interval improvement in degree of brain swelling was noted. LP done on the same day yielded turbid CSF, 1044 PMN leucocytes and 444 lymphocytes. No organisms were identified on Gram staining or grown on culture. Viral polymerase chain reaction (PCR) was positive for enterovirus and negative for herpes simplex viruses 1 and 2, as well as mumps virus. Biochemistry demonstrated elevated protein of 0.79g/L, low glucose of 2.7mmol/L (although there was no concurrent random blood glucose to compare with) and a normal chloride of 134mmol/L. The final diagnosis was 'most likely enterovirus encephalitis'.

Forty-seven patients (15.1%) of the 311 had interventions based on CT scan findings of which 40 (85.1%) required a CSF shunt (either new insertion, or revision of a previous VPS; or external ventricular drainage). Surgical drainage of brain abscess or subdural collection was indicated for four (8.5%) patients while the remaining three patients required therapeutic LP or ventricular tapping to relieve raised ICP in communicating hydrocephalus. Intervention was indicated in 25 (40.3%) of the 62 patients with CSF shunts compared to 22 (8.8%) of the 249 without CSF shunts; $p<0.001$. VPS revisions were carried out on two patients diagnosed with shunt sepsis and blocked shunt respectively although CT findings revealed no interval changes.

Eight (2.6%) patients, of whom two had normal CT, died during the admission. Causes of death were as follows: intracerebral haemorrhage due to undetermined causes, severe pneumococcal meningitis, suspected pineal mass, meningitis with subsequent cerebral herniation, complicated tuberculous meningitis and VPS malfunction with hydrocephalus. For the two with normal CT death followed severe pneumonia and acute liver failure secondary to hepatitis A.

Discussion

Our study shows that the majority of children who present with acute medical illness and undergo emergency head CT have no clinically significant findings on CT. The study also demonstrated that patients with CSF shunts made up a large proportion of patients undergoing head CT and were also more likely to be scanned repeatedly. Although this group comprised only 20% of the sample, it was significantly more likely to have abnormal CT findings and interventions based on CT findings. Patients with CSF shunts have previously been reported to have more investigations and surgical procedures in their lifetime [15]. In our study, a greater proportion of children with shunts required surgical intervention, compared to children without (40% versus 9%). This concurs with a longitudinal cohort study in the US by Florin et al., that demonstrated that 20% of 1319 patients with VPS presenting to the emergency department required surgical intervention [16].

Hydrocephalus (HCP) was the commonest CT finding, most likely reflecting the number of patients with CSF shunts who made up a large proportion of those undergoing the investigation and requiring intervention after imaging. Ventriculoperitoneal shunts (VPS), which are the commonest, are prone to numerous complications such as mechanical obstruction, malfunction, fracture, infection, migration and excessive CSF drainage [17]. A study in the United States analysed the long-term outcomes of VPS surgery in patients with HCP, with the primary outcome of interest being shunt failure [15]. It was demonstrated that 78.2% of the paediatric patients required shunt revision versus 32.5% in the adult population and this was statistically significant. Single shunt revision occurred in 21.3% of paediatric and 19.7% of adult patients. Multiple shunt revision occurred in 57.4% of paediatric and 12.7% of adult patients. The mean number of shunt revisions in children was 2.6 (range 0–17) and 0.6 (range 0–11) for adults. Patients with history of previous shunt surgery had

significantly greater shunt revision rates than those without previous shunt surgery (81.4% vs. 39.1%, $P < 0.01$). Statistically the odds for shunt revision in patients with prior shunt surgery were nine times higher than those without. Children were 4.22 times more likely to experience shunt revision [15].

Children with abnormal findings on first CT were more likely to present with abnormal clinical findings although a statistically significant association was manifest only with the presence of papilloedema or long tract signs. There was also a moderately strong association with nausea and vomiting. A cohort study performed on an adult American population found that in addition to altered mental status and focal neurology, papilloedema was a significant predictor of new intracranial pathology on CT scan [18].

In our study, seizures were the commonest indication for head CT. The median seizure duration was 15 minutes, with a predominance of generalised seizures. In 16.6% of the patients presenting with seizures a diagnosis of febrile seizures was made; all their CT imaging was normal. Other studies have also noted that patients with complex febrile seizures were more likely to receive an extensive workup, including a CT scan. In a study in Atlanta by Boyle and Sturm, of 53 patients with complex febrile seizures, none of the head CT scans performed showed significant findings that necessitated intervention or guided therapy [19]. This study excluded patients with CSF shunts; these patients were included in our study. In our study, of the cohort of 169 patients with seizures, we selected out 151 with no CSF shunts. In that group, 29.1% had abnormal findings on CT. The risk of abnormal CT findings was however not associated with the duration of seizures or whether the patients presented with focal or generalised seizures. This differs from a review of adult and paediatric studies by Harden et al., noting that focal seizures are likely predictive of abnormal CT results [20]. In

a previous study done at the same setting as our study, Swingler et al., concluded that routine CT imaging in children with recent onset partial seizures did not meaningfully change clinical management [13]. In New York, Maytal et al., studied the role of brain CT in evaluating children with new onset seizures in the ED [21]. A year-long retrospective review was done of case notes of all paediatric patients presenting with first-onset seizures to the ED who underwent brain CT was performed, excluding patients with simple febrile seizures. Of the 66 patients, 14 (21.2%) had abnormal results. The cause of seizures was deemed unknown in 33 patients, two of whom had abnormal results but neither warranted intervention. In 20 patients, 12 of whom had abnormal results, the cause was considered symptomatic. Two of the patients with abnormal results had findings of therapeutic significance which were foreseen from prior clinical evaluation. Of 13 patients with complex febrile seizures, none had an abnormal scan. Patients with partial seizures were more likely to have abnormal scans compared to those with generalised seizures, although the difference was not statistically significant. The authors concluded that routine brain CT scans for all patients with new onset nonfebrile seizures is not justified, and history and examination are enough to pick up patients warranting imaging. Another study by Allen and Jones, assessed children with epilepsy presenting with breakthrough seizures and undergoing head CT scanning [22]. Twenty-one children with breakthrough seizures were scanned. None of the scans had acute findings and they were all discharged from the emergency department, suggesting that the yield of emergent CT scans in epileptic children with breakthrough seizures is low. This corresponds with the recommendation by the American Academy of Neurology stating that emergency CT is not useful for patients with chronic seizure conditions [20].

Although children with seizure disorders are more likely to be scanned when they present with breakthrough seizures, available data indicate that they are unlikely to have new acute findings on CT. This is not surprising as children with chronic seizure disorders are likely to have been extensively

evaluated by neurologists and undergone previous investigations such as magnetic resonance imaging [22]. Most patients (65%) in our study with a prior diagnosis of epilepsy did not have clinically significant findings on CT. An evidence based review looking at both adults and children recommended that emergency CT not be undertaken for patients with chronic seizures [20]. It is possible that in our cohort of patients, which included a large proportion of children with CSF shunts, a shunt malfunction may have presented with breakthrough seizures.

In our study, the performance of CT to establish safety of LP in patients with suspected meningitis demonstrated a low yield of abnormal findings, with only two patients out of 70 noted to have radiological contraindications to LP. This is consistent with the findings of a prospective study by Gopal et al., involving 113 adults, in which only 2.7% had absolute radiological contraindications to LP [18]. Other investigators demonstrated that normal head CT results do not guarantee safety of LP in children with suspected raised intracranial pressure especially in the setting of bacterial meningitis [23, 24]. Acute meningitis may result in cerebral swelling and fatal herniation even without lumbar puncture [24]. An Australian study by Rennick, Shann and de Campo, looked at children with bacterial meningitis to assess whether the incidence of cerebral herniation increases immediately after lumbar puncture [24]. The authors concluded that there was a strong suggestion that LP may cause herniation in some patients, and normal CT results do not mean it is safe to perform a lumbar puncture in a paediatric patient with bacterial meningitis; clinical contraindications must not be ignored based on a normal CT result.

Normal head CT scans played a pivotal role in ruling out lesions and narrowing down the differential diagnoses. This made the emergency management of patients more efficient as the therapy was more targeted.

Relatively few decisions to scan were made by senior clinicians. It concerned us in this study that less than a third of decisions to do CT scan seem to have involved senior clinicians. This may be responsible for poor screening of patients. More senior input may be required before ordering scans. Over and above that, better clinical skills, especially checking for papilloedema, are vital in order to guide the scan requests and pick up subtle pathology clinically where scan results may otherwise be interpreted as normal.

Our study is limited by its retrospective design. In addition to missing data, due to the small sample size, the study was not powered to assess associations in a number of comparisons. Where univariate associations were noted, the small sample size precluded conducting of multivariable analysis to establish independent associations. Another limitation is that the study relies only on the radiologist's interpretation of CT findings and not on neurosurgical opinion which at times may differ from that of radiologists. Data on lumbar puncture opening pressures were largely missing with no documentation why they were not measured. It is not clear what contribution, if any, this clinical feature would have made towards findings and plan of management. Seizure duration, number of episodes and description of seizures and decision-makers in ordering CT scans are other missing data that may have proved useful.

Conclusion

Our study has found that most children presenting acutely to the MEU have normal or clinically insignificant findings on CT. Patients with VPS had the highest yield of abnormal scans with HCP the commonest finding. Our study also suggests the feasibility of creating a clinical selection tool that incorporates clinical features such as presence of nausea or vomiting, papilloedema and long tract

signs. This selection tool would require thorough clinical assessment to yield useful information. This is relevant because proper selection of patients for CT brain will reduce exposure of patients to unnecessary cranial irradiation, thereby reducing excess risk of malignancy. This is especially important for patients with CSF shunts who receive multiple CT imaging. Where CT is clearly indicated, the use of paediatric protocols with adjusted radiation doses and limited slice scanning will also assist in reducing radiation risk.

Head CT has revolutionized the diagnosis and management of illness in childhood, but possibly at the expense of good clinical skills and judgement. Thorough clinical assessment is still an indispensable and crucial tool in identifying patients that require CT brain.

Acknowledgements

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Appendices

Appendix 1: Head CT data collection sheet

1. PATIENT CHARACTERISTICS

	Study number:	Date of Folder Review _____/_____/20_____
1.1	Patient name	
1.2	Folder number	
1.3	Residence	
1.4	Date of birth	
1.5	Sex	Female ☐ Male ☐
1.6	Weight	
1.7	Origin	Clinic referral ☐ Secondary level ☐ Walk-in from home ☐ Trauma unit referral ☐
1.8	Triage classification	Red ☐ Orange ☐ Green ☐

2. CLINICAL FEATURES		
2.1	Date of admission/consultation	
2.2	Date of scan	
2.3	Index head CT or repeat scan	First time ☐ Repeat ☐
2.4	If repeat scan:	Number: _____ Previous scan(s) and indication(s):

2.5	Indications (As per CT request)	**i) Altered level of consciousness:** Yes ☐ No ☐ Not documented ☐ If yes, GCS (if documented): AVPU (if documented): **ii) Seizures:** Yes ☐ No ☐ Not documented ☐ If yes, Focal ☐ Generalised ☐ Atypical ☐ Not documented ☐ If atypical, specify: _____ Duration in minutes:_____ Not documented ☐ Number of episodes:_____ Not documented ☐ Witnessed: Yes ☐ No ☐ Not documented ☐ If yes, witnessed by: _____ Required anticonvulsants: Yes ☐ No ☐ Not documented ☐ If yes, which one(s): _____ **iii) Suspected VP shunt pathology:** Yes ☐ No ☐ No VP shunt in situ ☐ If yes, Blocked ☐ Infected ☐ Other (specify)_____ **iv) Raised intracranial pressure:** Yes ☐ No ☐ Not documented ☐ **v) Focal neurological deficit:** Yes ☐ No ☐ Not documented ☐ **vi) Other (specify):**
2.6	Associated symptoms (state duration where possible)	Headache: Yes ☐ No ☐ Not documented ☐ Drowsiness: Yes ☐ No ☐ Not documented ☐ Photophobia: Yes ☐ No ☐ Not documented ☐ Blurred vision: Yes ☐ No ☐ Not documented ☐ Tinnitus: Yes ☐ No ☐ Not documented ☐ Irritability: Yes ☐ No ☐ Not documented ☐ Apnoea: Yes ☐ No ☐ Not documented ☐ Vomiting: Yes ☐ No ☐ Not documented ☐ Nausea: Yes ☐ No ☐ Not documented ☐ Diarrhoea: Yes ☐ No ☐ Not documented ☐ Dizziness: Yes ☐ No ☐ Not documented ☐ Fever: Yes ☐ No ☐ Not documented ☐ Cough: Yes ☐ No ☐ Not documented ☐ Night sweats: Yes ☐ No ☐ Not documented ☐

		Weight loss/failure to thrive: Yes ☐ No ☐ Not documented ☐ Other:
2.7	Clinical signs	Vital signs (recorded at presentation or shortly after) Temperature _____ Heart rate _____ Blood pressure _____ Respiratory rate _____ Blood glucose _____ Oxygen saturation_____ Meningism: Yes ☐ No ☐ Not documented ☐ (as defined by neck stiffness, positive Kernig's or Brudzinski sign) Increased tone: Yes ☐ No ☐ Not documented ☐ Brisk tendon reflexes: Yes ☐ No ☐ Not documented ☐ Papilloedema: Yes ☐ No ☐ Not documented ☐ Unequal pupils: Yes ☐ No ☐ Not documented ☐ Cranial nerve palsy: Yes ☐ No ☐ Not documented ☐ If yes, specify _____ Motor deficit: Yes ☐ No ☐ Not documented ☐ If yes, specify_____ Sun-setting sign: Yes ☐ No ☐ Not documented ☐ Splayed sutures: Yes ☐ No ☐ Not documented ☐ Bulging fontanelle: Yes ☐ No ☐ Not documented ☐ Visible scalp veins: Yes ☐ No ☐ Not documented ☐ Chest crepitations: Yes ☐ No ☐ Not documented ☐ Head circumference and centile: Other significant sign(s):
2.8	Co-morbid condition(s)	Yes ☐ No ☐ Not documented ☐ If yes, specify:
2.9	Drug history	Nil of note ☐ Significant ☐ Not documented ☐ If significant, specify:
2.10	Past medical/surgical history	Nil of note ☐ Significant ☐ Not documented ☐ If significant, specify:
2.11	Family history	Nil of note ☐ Significant ☐ Not documented ☐ If significant, specify:

2.12	Birth history	Mode: Gestation: Birth weight: Apgars: Perinatal complications:
2.13	TB contact	Yes ☐ No ☐ Not documented ☐ -If yes, give details of contact and any investigations
2.14	HIV status	Negative ☐ Positive ☐ Exposed ☐ Unknown ☐
2.15	Immunisation status	Up to date ☐ Not up to date ☐ Not documented ☐
2.16	Development	Normal ☐ Delayed ☐ Not documented ☐
2.17	**PROVISIONAL DIAGNOSIS**	

3. HEAD CT SCAN INVESTIGATION		
3.1	Decision to scan made by:	i. Consultant ☐ ii. Senior Registrar ☐ iii. Paediatric Registrar ☐ iv. Medical Officer ☐ v. Intern ☐ vi. Other ☐ vii Cannot be ascertained ☐
3.2	Time of ordering of scan	
3.3	Time the scan was performed	
3.4	Time interval	
4. PRE-SCAN MANAGEMENT		
4.1	Investigations	Lumbar puncture: Yes ☐ No ☐ Not documented ☐ Time (if documented): Results: Full blood count: Yes ☐ No ☐ Not documented ☐ Results: C reactive protein: Yes ☐ No ☐ Not documented ☐ Results: Urea, electrolytes&creatinine: Yes ☐ No ☐ Not documented ☐ Results: Blood culture: Yes ☐ No ☐ Not documented ☐ Results: Tuberculin test: Yes ☐ No ☐ Not documented ☐ Result: Positive ☐ Negative ☐ Not documented ☐

		Induced sputum/gastric washings (specify which one if done): Yes ☐ No ☐ Not documented ☐ Chest radiograph: Yes ☐ No ☐ Not documented ☐ Results: EEG: Yes ☐ No ☐ Not documented ☐ Results: Other investigation(s):
4.2	Medication	Antibiotics: Yes ☐ No ☐ Not documented ☐ Details: Medication(s): Time commenced: Anti-TB therapy: Yes ☐ No ☐ Not documented ☐ Details: Medication(s): Time commenced: Systemic corticosteroids: Yes ☐ No ☐ Not documented ☐ Details: Medication(s): Time commenced: Antiviral therapy: Yes ☐ No ☐ Not documented ☐ Details: Medication(s): Time commenced: Anticonvulsants: Yes ☐ No ☐ Not documented ☐ Details: Medication(s): Time commenced: Other (mannitol, hypertonic saline): Yes☐ No ☐ Not documented ☐ Details: Medication(s): Time commenced:
5. HEAD CT RESULTS		
5.1	Findings	No intracranial pathology ☐ Hydrocephalus (specify whether (non)communicating) ☐ Cerebral oedema ☐ Cerebral atrophy ☐ Thrombosis(specify) ☐ Space occupying lesion (specify) ☐ Meningitis (specify) ☐ Infarct ☐ Haemorrhage ☐ Other (specify) ☐

		Extracranial abnormalities ☐
5.2	Was further imaging indicated?	i. Yes ☐ ii. No ☐
5.3	Did the patient subsequently have further imaging within 24 months after this scan?	i. Yes ☐ ii. No ☐ If yes, specify:

6. POST-SCAN MANAGEMENT		
6.1	Investigation	Lumbar puncture: Yes ☐ No ☐ Not documented ☐ Date, time and result: Other investigation (specify and document result if applicable)
6.2	Medication	Antibiotics: Started ☐ Continued ☐ Changed ☐ Stopped ☐ Never started ☐ Anti-TB: Started ☐ Continued ☐ Changed ☐ Stopped ☐ Never started ☐ Corticosteroids: Started ☐ Continued ☐ Changed ☐ Stopped ☐ Never started☐ Antiviral: Started ☐ Continued ☐ Changed ☐ Stopped ☐ Never started ☐ Anticonvulsants: Started ☐ Continued ☐ Changed ☐ Stopped ☐ Never started ☐
6.3	Intervention	Yes ☐ No ☐ Not documented ☐ If yes, specify:
6.4	**FINAL DIAGNOSIS**	

7. OUTCOME	
Discharged ☐ Died ☐	Date:
Transferred ☐	Date:

Outcome post-transfer: Dicharged ☐ Died ☐	Date:
Follow up plan(s)	

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Appendix 2: HREC UCT Ethics approval

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E52-24 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492 • **Facsimile** [021] 406 6411
Email: Sumayah.ariefdien@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

12 March 2015

HREC/REF: 087/2015

Dr H Buys
Paediatrics, Ambulatory & Emergency
5th Floor ICH Building
Red Cross Children's Hospital
Rondebosch

Dear Dr Buys

Project Title: THE CLINICAL USE AND INDICATIONS FOR BRAIN CT SCANS IN PAEDIATRIC AMBULATORY CARE (SHORT STAY WARD AND MEDICAL EMERGENCIES) AT A CHILDREN'S HOSPITAL OVER A ONE YEAR PERIOD, 1ST JANUARY - 31ST DECEMBER 2013

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above mentioned study.

Approval is granted for one year until the 28 March 2016.

Please submit a progress form, using the standardised Annual Report Form, if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.

Please note that the on-going ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the HREC REF in all your correspondence.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, HSF HUMAN ETHICS

Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

Hrec/ref:088/2015

Appendix 3: Annual progress report/renewal

UNIVERSITY OF CAPE TOWN

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

FHS017: Annual Progress Report / Renewal

Record Reviews/Audits/Collection of Biological Specimens/Repositories/Databases/Registries

HREC office use only (FWA00001637; IRB00001938)			
This serves as notification of annual approval, including any documentation described below.			
☑ Approved	Annual progress report	Approved until/next renewal date	30.8.2017
☐ Not approved	See attached comments		
Signature Chairperson of the HREC		Date Signed	16/8/2016

Principal Investigator to complete the following:

1. Protocol information

Date (when submitting this form)	28/07/2016		
HREC REF Number	087/2015	Current Ethics Approval was granted until	28/03/2016
Protocol title	THE CLINICAL USE AND INDICATIONS FOR HEAD CT SCANS IN PAEDIATRIC AMBULATORY CARE (SHORT STAY WARD AND MEDICAL EMERGENCIES) AT A CHILDREN'S HOSPITAL OVER A ONE YEAR PERIOD, 1ST JANUARY-31ST DECEMBER 2013		
Principal Investigator	DR HELOISE BUYS		
Department / Office Internal Mail Address	DEPARTMENT OF PAEDIATRICS		
1.1 Does this protocol receive US Federal funding?		☐ Yes	☑ No

2. Protocol status (tick ✓)

☑	Research-related activities are ongoing
☐	Data collection is complete, data analysis only
Please indicate (in the block below) the titles and HREC reference numbers of any projects currently making use of the Database/registry/repository	
NOT APPLICABLE	

3. Protocol summary

Total number of records or specimens collected, reviewed or stored since the original approval		174
Total number of records or specimens collected, reviewed or stored since last progress report		174
Have any research-related outputs (e.g. publications, abstracts, conference presentations) resulted from this research? If yes, please list and attach with this report	☐ Yes	☑ No

4. Signature

Signature of PI		Date	10/08/2016

Appendix 4: Hospital Management (RCWMCH) Approval

Western Cape Government
Health

Dr AS Booysen
Manager: Medical Services
Email: Tony.Booysen@Westerncape.gov.za
Tel: +27 21 658 5788 fax: +27 21 658 5166

Dr H Buys
Red Cross War Memorial Children's Hospital

Dear Dr H Buys

APPROVAL OF RESEARCH

PROJECT TITLE: THE USE OF BRAIN CT SCANS IN PAEDIATRIC AMBULATORY CARE (SHORT STAY WARD AND MEDICAL EMERGENCIES

It is a pleasure to inform you that approval is hereby granted to conduct the above-mentioned study at Red Cross War Memorial Children's Hospital.

Yours sincerely,

Dr AS Booysen
Manager: Medical Services
Date: 27.11.15

Appendix 5: PLOS One journal instructions to authors

PLOS ONE

TITLE, AUTHOR, AFFILIATIONS FORMATTING GUIDELINES

This is the article title

John Doe[¶], Antonie Data[¶], Johannes van Stats[1,#a], Marie Testperson[2*], David Ribosome Jr.[3,5], Gregory H.T. McBio[4,#b], Angela Revieweron[1,2&], Marina Measure[1&], on behalf of The Bunny Genome Sequencing Consortium[^]

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[&]These authors also contributed equally to this work.

[^]Membership of the Bunny Genome Sequencing Consortium is provided in the Acknowledgments.

Symbol Legend		
Symbol	Name	Definition
¶	Pilcrow (paragraph symbol)	1st set of equal contributors
&	Ampersand	2nd set of equal contributors
*	Asterisk	Corresponding author(s)
#a	Pound/number sign	First Current address
#b	Pound/number sign	Second Current address
†	Dagger/Cross	Deceased
^	Caret	Consortium/Group Authorship

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Author Byline
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Abstract

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Introduction

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Materials and methods

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$$p^2 + 2pq + q^2 = 1 \quad (1)$$

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Genotyping

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Whole genome RFLP analysis

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Results and discussion

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Table 1. This is the Table 1 Title.

	Chemical W	Chemical X	Chemical Y	Chemical Z
Chemical 1	Reaction 1W	Reaction 1X	Reaction 1Y	Reaction 1Z
Chemical 2	Reaction 2W	Reaction 2X	Reaction 2Y	Reaction 2Z
Chemical 3	Reaction 3W[a]	Reaction 3X	Reaction 3Y[b]	Reaction 3Z
Chemical 4	Reaction 4W	Reaction 4X	Reaction 4Y	Reaction 4Z
Chemical 5	Reaction 5W	Reaction 5X	Reaction 5Y	Reaction 5Z

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Acknowledgments

- Do not include funding or competing interests information in Acknowledgments.

References

1. Doe J, Data A, van Stats J, Testperson M, Ribosome D Jr, McBio GHT, et al. This is the article title. PLoS ONE. 2017;12(12):e00000. doi: 10.1371/journal.pone.0000000
2. Doe J, Data A, van Stats J, Testperson M, Ribosome D Jr, McBio GHT, et al. Bunny dynamics in cartoon landscapes. PLoS ONE. Forthcoming 2017.

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