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Development and Evaluation of the Manufacture of a Coronary Stent for the South African Market

Markus Lehmann

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DECLARATION

I, Markus Lehmann, declare that the work set out in this thesis is essentially my own work and that no part has been submitted for a degree at any academic institution

Signed by candidate

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Markus Lehmann

Cape Town, February 2000

SYNOPSIS

The need for economic treatment of coronary heart disease in South Africa and the popularity of coronary stent implantation as an effective treatment increases. Stent implants have had to be imported to date with significant cost involved. The project in hand therefore deals with the evaluation of the possibilities of economical local manufacture of a coronary stent.

The design of several coronary stents currently in use was carefully analysed and the results of clinical application described in the literature were reviewed. After evaluating the patent situation, a suitable design concept was chosen, based primarily on the availability of manufacturing equipment. The design concept of choice is the balloon expandable slotted tube variety. Stents of this most popular slotted tube design are usually laser cut out of a tube with good results. Since there was no suitable laser cutting equipment in use in South Africa, it was undertaken to manufacture stent prototypes by spark erosion to establish the general suitability of the method for stent manufacturing. The initial design was adjusted several times to the manufacturing process and suitable machine parameters were evaluated. For comparison a stent of a similar design was laser cut by an established European manufacturer. The geometry of the most favourable prototypes was analysed by computer simulation using finite element analysis, followed by simple physical tests of deployment and radial strength. The quality of manufacturing was evaluated with electron microscopy.

The computational and mechanical test results of the design analysis yielded largely satisfactory results, but it was found that the manufacturing process of spark erosion is not suitable to manufacture products that would have to compete on the current sophisticated market. With the spark erosion equipment, neither a satisfying surface quality nor acceptable geometrical tolerances could be achieved. This was particularly obvious after comparison with the laser cut stent sample of the same design. An improvement in quality of the spark erosion process would require extensive fine-tuning and would increase the already very long manufacturing time and the cost significantly. Subcontracted laser cutting in Europe was found to be more reliable and economical.

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CHAPTER ONE

INTRODUCTION

From the early decades of the 20th century, coronary heart disease has established itself as the main cause for death and disability in industrialised nations. Although it has been the major disease burden of modern societies since the 1920's, it had little significance in developing countries and societies until about twenty years ago (Walker, 1999). Over the past ten years the situation has started to change dramatically. With the advance of access to Western life style nutrition and habits, like smoking and lack of exercise, the occurrence of coronary heart disease within developing societies is rapidly catching up with numbers known from the Western world. The World Health Organisation predicts that ischaemic heart disease will account for the majority of deaths and disabilities world-wide as soon as the year 2020. This trend is also reflected in South Africa. The 'Western way of death' (van Rensburg *et al.,* 1982) has been described as practically non existent amongst black Africans by several authors (Seftel, 1978, Walker, 1999) while being the major cause of death threatening the Westernised parts of the population until the early eighties. The situation in South Africa has changed since then. With a growing portion of its formerly developing societies having access to wealthy lifestyles and people reaching a higher age, the occurrence of arterial ischaemic disease, and coronary arterial ischaemic disease in particular, is increasing (Bradshaw *et al.,* 1999).

Myocardial infarction, more commonly referred to as "heart attack", is normally caused by the blockage of a coronary artery. In most cases it is preceded by a history of symptoms like angina pectoris - or chest pain - a sign of insufficient blood supply to the heart muscle, resulting from the reduction in luminal diameter of the coronary arteries. The disease is chronically progressive and coronary arteries narrow from patches of arteriosclerotic plaque deposited inside the vessel walls, which in turn causes increasing incapacity from angina. The condition can – in its severest form – lead to a complete shutdown of blood flow to areas of the heart muscle and myocardial infarction. Often, cardiac death is the result.

Treatment includes the use of anticoagulant drugs to secure efficient blood flow, several mechanical approaches to re-open the vessel or surgery to bypass a restricted or occluded coronary artery. In many cases the more cost effective and safer interventional techniques are an attractive alternative to bypass surgery. Most popular among these techniques is Percutaneous Transluminal Coronary Angioplasty (PTCA). In this technique an inflated balloon, making up the tip of a catheter, is deployed inside the narrowed vessel segment. The inflated balloon stretches out the artery radially, thus creating a bigger cross-sectional diameter. The major drawback is the general tendency of elastic recoil and restenosis of the dilated vessel.

In 1969 Charles Dotter published a new technique called intravascular stenting to overcome the recoil of treated stenotic arteries. An endovascular spiral stent was successfully placed inside a vessel after the restricted segment was treated by percutaneous transluminal angioplasty. However, since the technical possibilities of imaging were still limited it was not before the late 1980's that this method could be routinely used.

Currently the most popular treatment for coronary artery restriction is coronary stenting. A tubular, deployable, metallic implant is introduced into the prewidened artery segment and deployed to a larger diameter to reinforce it and prevent elastic recoil (Figure 1.1). The stent implant (Figure 1.2) stays inside the vessel permanently. Stenting has been shown to represent a safe and economic method of arterial revascularisation (Cleland *et al.;* 1995; Cohen *et al.,* 1993 and 1994; Fischmann *et al.,* 1994; Keane, 1995; Marco 1998, Serruys *et al.,* 1994). More than 400 000 Americans and 800 000 patients world-wide undergo a non-surgical coronary artery interventional procedure each year. Although stenting for coronary arteries was only introduced in the 1990s, in some laboratories intracoronary stents are used in more than 50% of the patients (Pepine *et al.,* 1996). Meanwhile, stenting of larger peripheral vessels, like iliac, femoral, renal or carotid arteries has also become a standard treatment (Henry *et al.,* 1998) and a large variety of shapes and sizes of peripheral stents are available.

Several design concepts for coronary and other stents have been developed since the early 1980s, some of them even being spring loaded to self-expand at the desired location. However, the balloon expandable, so-called corrugated ring design has established itself as being the design of choice for most of the coronary stents currently on the market. Here, an arrangement of openings in a surgical grade stainless steel tube allows the change of the tube diameter to occur by the plastic deformation of the latticework structure when an internal or external pressure is applied (Figure 1.2).

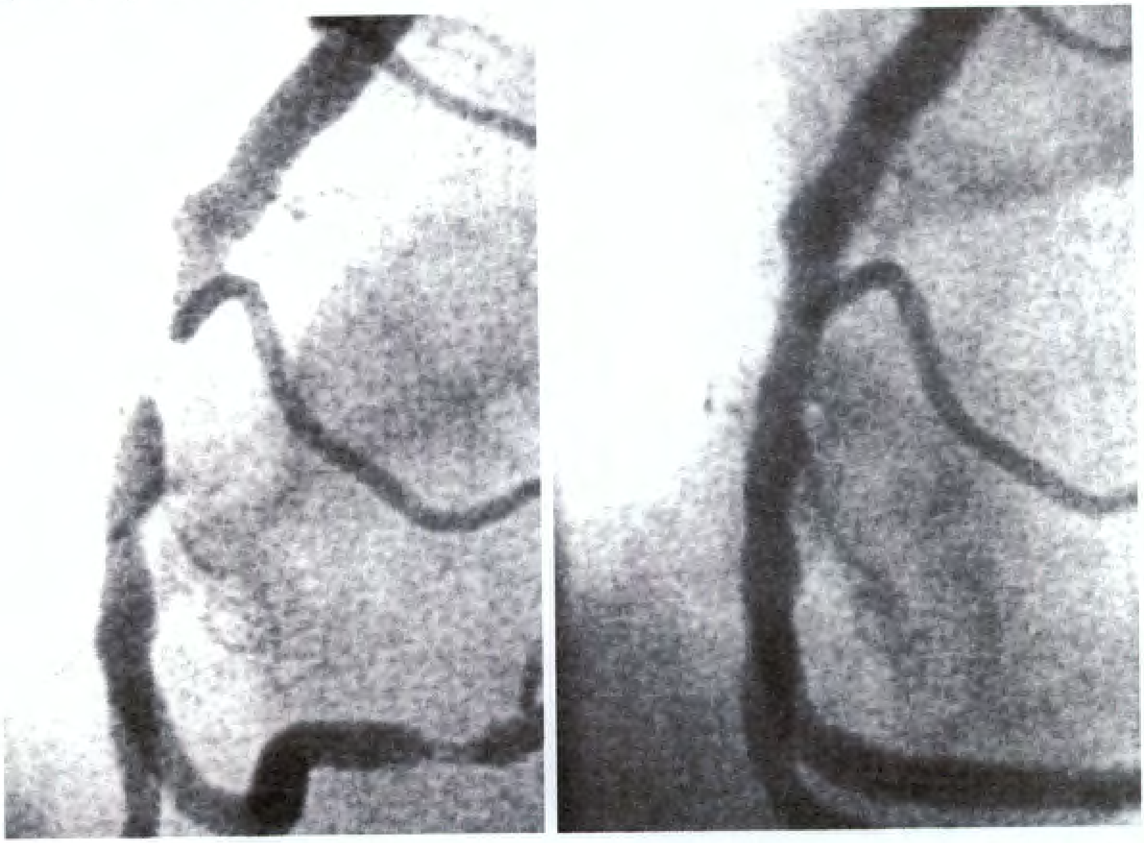
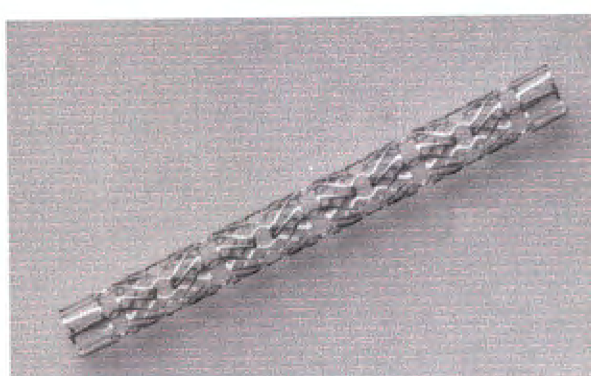


Figure 1.1 Angiogram of a stenosed right coronary artery before (left) and after PTCA followed by stenting (right).



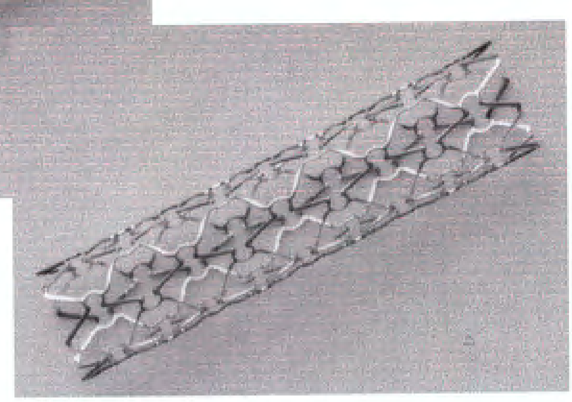


Figure 1.2
Typical coronary stent[1.1]*.*
Non-expanded (left)
and expanded (right)
(images: CardioVascular Dynamics).

Several factors, such as the poor Rand exchange rate, import taxes, high labour costs in Western countries and the cost of international approval of world-wide

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[1.1] FOCUSTENT Enforcer™, Cardio Vascular Dynamics, Inc, California, USA.

distributed medical devices make these stents, which are exclusively imported, unnecessarily expensive in South Africa. One way of eliminating this factor is to manufacture stents locally for exclusive distribution in South Africa.

The rising demand for coronary stents in South Africa, together with the future predictions of coronary arterial disease in this country and the current high cost of those implants, are the motivation for this project. It is intended to evaluate a possible way of providing the South African market with stents that are notably cheaper than imported products by manufacturing them locally.

Except for very few exotic exceptions, the manufacturing of the most successful corrugated ring slotted tube stents is done by laser cutting the structure followed by an electrochemical polishing process. At present there is no suitable laser cutting equipment available in South Africa to cut the very fine structure for coronary stents out of a stainless steel tube. However, there is spark erosion equipment that seemed suitable for stent manufacture and it was decided to evaluate this method as a possible alternative to laser cutting stents and thereby make the local manufacture of stents possible.

For this project a number of prototypes will be manufactured by spark erosion. An initial review of literature including the evaluation of the variety of currently available coronary stents will form the foundation for the definition of a general design concept and the required design parameters. Based on these findings a coronary stent, suitable to be manufactured by the proposed technique, will be designed and prototyped. This design will not only be used to test the general suitability of spark erosion but also to adjust the process and improve machining parameters for the manufacture of larger volumes of stents. In addition, the design will probably have to undergo some adjustment to the spark erosion process as prototyping progresses. The manufactured prototypes will subsequently undergo basic testing to validate the design and the manufacturing technique. These tests include comparative simulated and experimental tests of stent deformation by performing a computer simulated deployment and a physical deployment of a prototype on a PTCA balloon. Radial compliance tests will make it possible to compare the performance of this stent to that of other stents. Finally electron microscopy imaging will be used to evaluate the overall quality of the spark eroded stents and compare them to state of the art laser cut specimens of a similar design.

CHAPTER TWO

REVIEW OF LITERATURE

2.1 Pathology of Ischaemic[2.1] Heart Disease

The cardiovascular system consists mainly of the heart as a pump and the blood vessels as a network of pipes, forming a closed circulatory system. Pulsating contraction and dilatation of the muscular heart walls, the myocardium[2.2], together with the action of valves between the heart chambers and at the outlets of the heart, make up the pumping performance of the heart, or the "heart beat". It is rhythmically repeated throughout life on at least 60 to 70 times a minute (or about 100,000 times per day) by the co-ordinated action of millions of muscle cells of the myocardium. The heart output is a function of the frequency and strength of myocardial contractions and varies from about 5-7 litres/minute to up to 30 litres/minute in athletes during activity. Damage to any area of the myocardium affects its contractile activity and the heart's performance. Each myocardial cell is supplied with nutrients and oxygen by the coronary[2.3] arterial system, which originates from two openings in the wall of the aorta as it leaves the heart (Figure 2.1). These arteries branch out extensively over the surface of the heart to supply the whole of the myocardium. Coronary blood flow in healthy coronary arteries can increase several times in response to increased myocardial work.

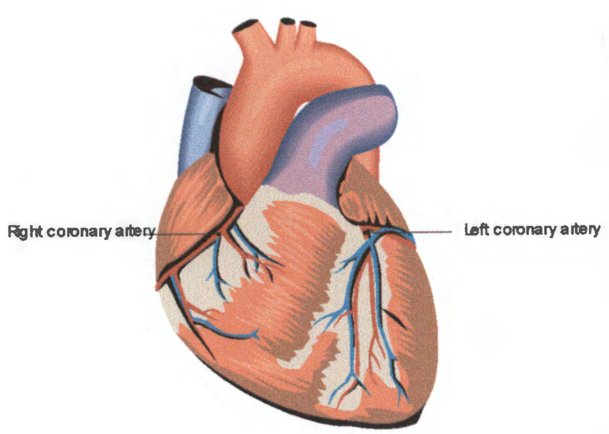


Figure 2.1
The main coronary arteries supplying the heart muscle.

[2.1] ischein, Gk.: holding back; aemie, Gk.: blood
[2.2] myo, Gk.: muscle; kardia, Gk.: heart.
[2.3] corona, L.: rim.

Coronary artery stenosis[2.4] restricts the arterial blood supply of the myocardium in ischaemic heart disease. Arteriosclerotic[2.5] changes in the coronary arteries and changes in the blood can cause an arterial stenosis or occlusion.

Arteriosclerosis is thickening and hardening of the arterial walls and is caused by the deposition of fatty substances and cholesterol inside the arterial lumen. The thickened areas are usually found in patches of varying size, decreasing the vessel diameter. Arteriosclerosis is a chronic disease that slowly advances with age and can cause varying degrees of narrowing and even complete occlusion of the vessel resulting in obstruction of blood flow. It causes the clinical syndromes of ischaemic heart disease in over 90% of patients (Schoen, 1989).

Reduction of the luminal cross-sectional area by 75% leads to a lack of oxygen supply during increased myocardial demand (e.g., exercise). A reduction by more than 90% restricts coronary flow at rest (Schoen, 1989). The first symptom of ischaemic heart disease is therefore usually chest pain, *angina pectoris*[2.6] during increased physical activity.

A sudden formation of an occlusive thrombus[2.7] in unstable arteriosclerotic plaques can trigger myocardial infarction. The former chronic ischaemic heart disease then turns into the acute condition known as 'heart attack'.

Infarction occurs when the blood supply to the myocardial areas is so restricted that it leads to irreversible cell damage and loss of contractile force. The effect of the infarction on the function of the heart, largely depends on the size and position of the damaged myocardial areas and ranges from minor impairment to heart performance, when only small and less important areas of the myocardium are affected, to complete heart failure.

[2.4] steno, Gk.: narrow; osis, Gk.: disease.
[2.5] arteri, Gk.: artery; scler, Gk.: hard, dry.
[2.6] angere, L: restrict; pectus, L: breast.
[2.7] thromb, Gk.: thickly liquid drop, bloodclot.

2.2 Treatment of Ischaemic Heart Disease

Ischaemic heart disease is treated by restoring adequate arterial blood flow to insufficiently supplied myocardial areas. This is most successfully done during the chronic phase of the disease before myocardial damage occurs. Following acute myocardial infarction, early and long-term mortality correlates strongly with the amount of residual functioning myocardium (Schoen, 1989). Although anticoagulant drugs play a useful part in preventing some of the short term complications of coronary heart disease they have a weak effect, if indeed any, on the prevention of further coronary attacks (Cleland *et al.*, 1995). To improve the long-term life expectancy of the patient and prevent the occurrence or repetition of an acute infarction, the arteriosclerotic stenosis of the artery must be treated. At present there are different surgical and interventional approaches that deal with the biological problem of ischaemic coronary disease. *Surgical* techniques, access the diseased vessel by open-heart surgery. In contrast, *interventional* techniques are minimally invasive. In these techniques catheters, introduced through a large peripheral artery, are used to access the diseased artery.

In general the treatment options are:

- *surgical* revascularisation by bypassing the restricted segment with an artificial piece of vessel
- *interventional* removal of part of the arteriosclerotic plaque (atherectomy)
- *interventional* widening of the stenosis

2.2.1 Interventional Techniques

Removal of the arteriosclerotic plaque is a logical approach to the biological problem of vessel stenosis. Several devices and techniques have been developed to do this, such as the directional coronary atherectomy (DCA), the transluminal extraction catheter atherectomy or the artery rotablation. In all those plaque is shaved off with rotating cutting devices. Laser angioplasty has also been successfully tested. Besides the drawback of danger of vessel wall injury with all these techniques, most devices are relatively bulky and stiff and can therefore only be used in large, straight vessels with a diameter larger than 3mm.

The commonly used interventional technique for revascularisation is PTCA, first performed by Andreas Gruentzig in 1977 (Cleland *et al.*, 1995, Gruentzig *et al.*, 1979). A catheter with a distal balloon is inserted into the restricted vessel segment. The balloon is inflated to the original vessel diameter to widen the restriction, thereby creating a bigger lumen and restoring normal flow within the vessel (section 2.2.2).

The described interventional methods, especially PTCA, have been shown to be economically favourable treatments in comparison to coronary artery bypass grafting (CABG). This is based on the fact that CABG is a large and complex surgical procedure, which requires a high use of resources. In addition, the total cost is higher due to significantly longer hospitalisation of the patients (Cohen *et al.,* 1993 and 1994). Using interventional methods, the patient is usually only treated with local anaesthetics and can be released from hospital within one or two days. CABG only seems justifiable where there is multiple stenosis of the coronary arterial system, when re-opening of only a few stenoses would not have the desired curative effect or where stenoses are located in positions that cannot be treated by interventional techniques.

None of the first mentioned atherectomy methods seem to have a large clinical significance for primary treatment (Cleland, 1995) but do get used in conjuction with PTCA and stenting (Bonnier, 1998, Garcia, 1998; Köster *et al.,* 1998; Louvard *et al.,* 1998; Margolis, 1998; Schiele *et al.,* 1998). Studies demonstrate that there is no clinical benefit from atherectomy compared with PTCA (Topol *et al.,* 1994). Although removal of the arteriosclerotic plaque, rather than simply dilating the vessel, seems an attractive concept, PTCA must be considered the preferred approach, since atherectomy presents a significantly higher early complication rate (Topol *et al.,* 1994). The results throughout the literature indicate that PTCA is the most successful interventional technique, both clinically and economically (Cleland *et al.*, 1995).

Nevertheless, limitations of PTCA have been recognised. Elastic recoil of the artery or artery dissection, both followed by restenosis, often impair the success of the technique.

The muscular arteries tend to contract and re-close after the dilatation catheter has been withdrawn. Since the plaque is not removed in the first place, the former biological problem now also encompasses a biomechanical component. Balloon over dilatation was proposed to overcome elastic recoil of the vessel by stretching the muscular layer but this method often leads to dissections of the vessel wall. Dissection of the artery followed by thrombus formation and abrupt occlusion of the vessel is a common complication (Castañeda-Zúñiga *et al.,* 1992).

The technique of coronary arterial stenting is now used to overcome the drawbacks of restenosis and abrupt occlusion after PTCA. It therefore has to be looked at as being a further development of the PTCA technique.

2.2.2 Coronary Stenting

A stent opposes the elastic recoil of vascular stenoses and provides internal vessel wall support. This metal coil-like or slotted tubular structure gets permanently implanted into the artery. The method is therefore a mechanical approach to a biomechanical and biological problem. Although it does not solve the biological problem of the arteriosclerotic deposits inside the vessel, it addresses the biomechanical problem of reclosure of the vessel after PTCA and at least reduces the effect of the biological problem.

Prior to stent placement, the diseased vessel segment is normally widened by PTCA. To reach the coronary artery and to deliver contrast medium for angioraphy[2.8] to the diseased vessel, a tube like guiding catheter is introduced into a large peripheral artery of the body. In most cases the femoral artery is used, since it is easily accessible being superficial in the groin region. In some cases the brachial or radial artery is used instead (e.g., when the femoral arteries are restricted in elderly patients). Under x-ray vision, the catheter is pushed into the aorta and the distal tip placed at the entrance to the coronary artery. Contrast medium is then injected for a diagnostic angiogram to evaluate the sites and grades of the stenoses (Figure 2.2). A thin, rigid wire, typically less than 0.4mm in diameter, is inserted through the guiding catheter into the diseased artery (Figure 2.3a). This highly radiopaque and torque transmitting guidewire serves as a track to guide the various balloon catheters to the target site.

[2.8] Angiography is an X-ray imaging technique used for blood vessels. The arteries are filled with a radiopaque medium to make them visible on an X-ray image (Hoxter *et al.,* 1991). It should be noted that angiography is an indirect imaging method since the image does not show the vessel itself but the distribution of fluid inside the vessel (Figures 2.2 and 2.5).

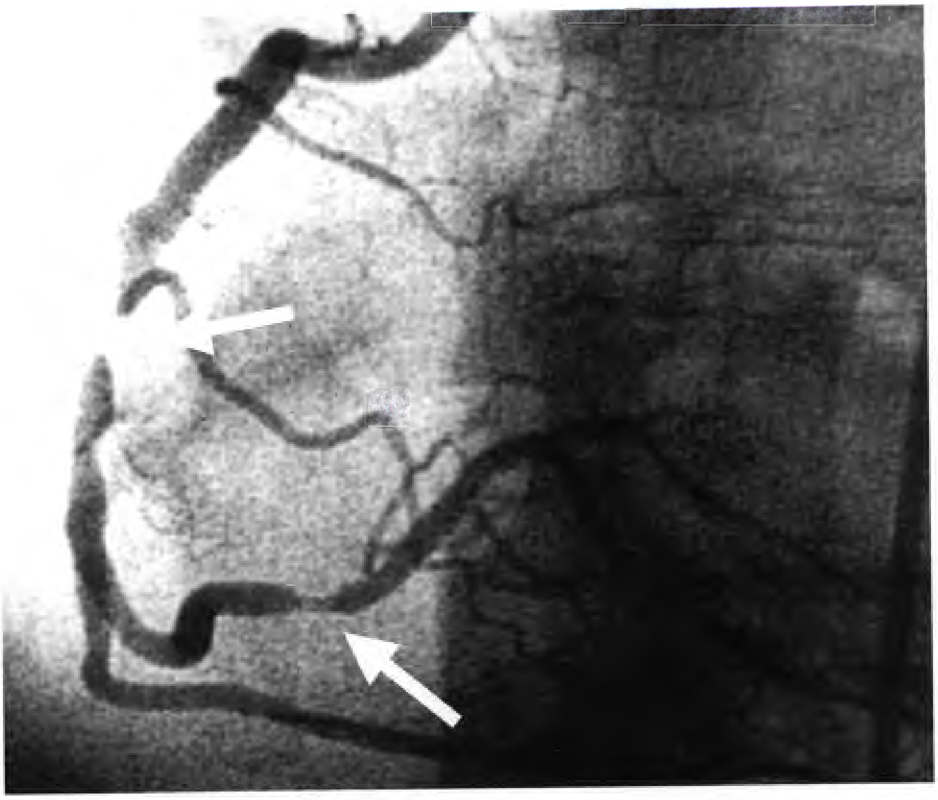
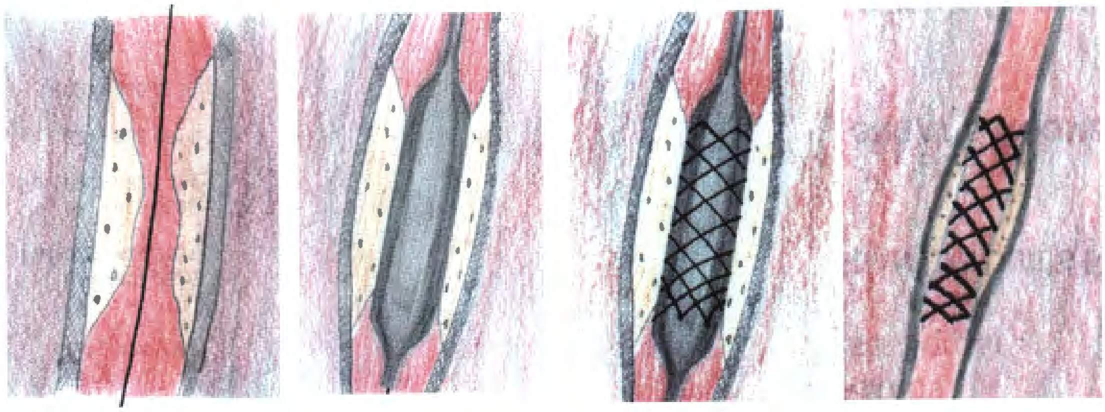


Figure 2.2 An angiogram of a diseased coronary artery. Narrowings of the blood vessel can be seen indirectly (arrows), where the contrast medium is distributed poorly due to arteriosclerotic plaque inside the vessel lumen.

A PTCA balloon is now delivered to the site of the stenosis by pushing it over the guidewire. The correctly positioned balloon is inflated and widens the stenosis inside the arterial lumen (Figure 2.3b).

A stent implant is placed at the site of the former stenosis to avoid vessel recoil. The delivery depends on the kind of stent used. Self-expanding stents (section 2.4.1) are spring loaded and pre-mounted onto the delivery catheter. Balloon expandable stents (section 2.4.2) are crimped onto a conventional angiography balloon. In both cases the catheter is pushed over the guidewire to the target site. While the self-expanding stent is released from its spring-loaded state off the catheter, inflating the PTCA balloon deploys the balloon expandable stent. The expanded stent presses against the vessel wall with its diameter being continuous or slightly larger than the nominal vessel diameter (Figure 2.3c). The delivery catheters are withdrawn and the stent implant remains inside the artery providing patency by scaffolding the vessel walls (Figure 2.3d and 2.4).



a b c d

Figure 2.3 *a) Insertion of a guidewire into the diseased vessel. b) Prewidening of the stenosis by an angioplasty balloon. b) Placement of the stent implant. d) The stent remains inside the artery providing patency.*

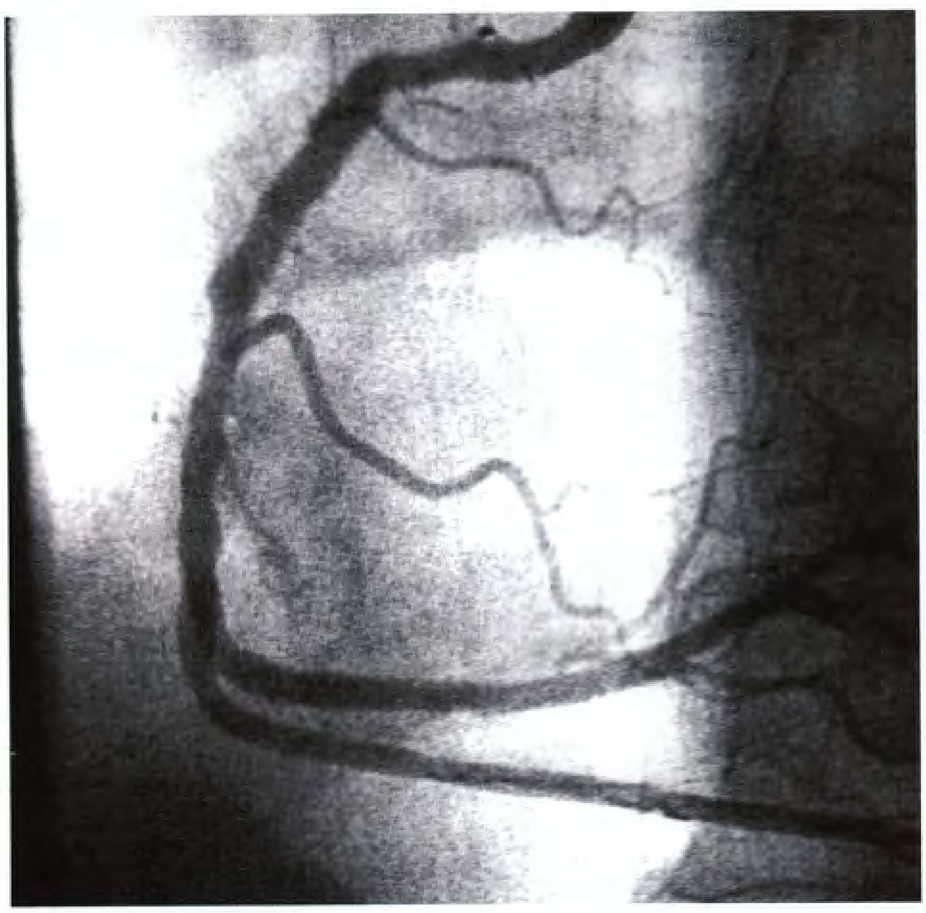


Figure 2.4 *An angiogram of the stented coronary artery from Figure 2.2*

An intravascular stent, placed immediately after performing a conventional PTCA, primarily prevents the elastic recoil of the vessel by holding it open to a predetermined diameter. In addition it also corrects possible effects of vessel dissection caused by overdilating the PTCA balloon. The stent keeps the dissected layers back against the arterial wall (Marco, 1998; Palmaz, 1992).

Since the introduction of intravascular stenting in the 1980s and coronary stenting in the early 1990s, the technique has developed rapidly. In fact, intracoronary stenting is now used in more than 50% of the patients undergoing non-surgical coronary artery interventional procedures each year (Pepine et al., 1996). Initial enthusiasm for the use of stents was tempered by the high acute occlusion rate but, improved stent design, deployment at high pressures and careful anticoagulation regimens have significantly reduced this serious complication (Cleland et al., 1995).

Comparisons between coronary stent placement following PTCA and PTCA only for treatment of myocardial ischaemia have been performed in several clinical trials (Fischman *et al.,* 1995; Macaya *et al.,* 1996; Serruys *et al.,* 1995). It was found that the immediate outcome according to the analysis of clinical events (restenosis, myocardial infarction) was similar in both the stented patient group and the patient group that underwent only the PTCA procedure. The long-term re-stenosis rates, however, were significantly lower in the stented patient group than they were in the patient group that underwent PTCA only. The reduction in clinical events was mainly due to a reduced need for a second PTCA in the stented patient group. It was shown that the minimum residual luminal diameter immediately after the procedure and at six or seven months was significantly larger in the stented group (Fischman *et al.,* 1995; Serruys *et al.,* 1995).

In summary the results show that coronary stenting of selected patients reduces the re-stenosis and re-intervention rates in the short and medium term (Marco, 1998). The very long-term effects of stenting within a coronary artery are still not known (Topol, 1994) although there are now limited data available, indicating a high success rate after 9 years (Karam C, 1998).

2.3 Coronary Stenting in South Africa

2.3.1 Epidemiology

Ischaemic heart disease is one of the most important health problems facing the developed countries of the world, where it accounts for the majority of all deaths. The disease occurs due to many factors mainly appearing within a society with a "Western" life style and standard of living. The term "Western" life style in this context means the typical nutritional metabolic milieu and other factors found mainly in civilised "Western" societies. These factors include mature age, male sex, diabetic and genetic disorders, high cholesterol levels caused mainly by a high intake of saturated fats, smoking, lack of exercise, and high blood pressure (Shillingford, 1981; van Rensburg *et al.,* 1982).

South Africa has the dubious reputation of having the world's highest death rate from ischaemic heart disease and this applies throughout society, only with the black population group still being the exception. There is currently no accurate data on the incidence of cardiovascular disease in South Africa (Bradshaw *et al.*, 2/1999) but in 1989 the proportion of total deaths due to cardiovascular disease in South Africa was reported to be 20.1%, with 30.2% of them caused by ischaemic heart disease (Murray, 1990). In 1991 29,692 deaths were caused by cardiovascular disease; 10,475 of them were white men and 4,766 white women (Pestana *et al.,* 1996). Meanwhile an increased standard of living, has lead to an increase in the disease rate in the black population group. In comparison with the rest of that population group, it appears that black patients with myocardial infarction have already been considerably "Westernised" (Bradshaw *et al.*, 4/1999; van Rensburg *et al.,* 1982). In 1985 4.9 million South Africans smoked, the largest group of smokers (2.6 million) being black males. 5.5 million South Africans had blood pressures above 140/90mmHg; again the largest group (3.0 million) was black (Steyn *et al.,* 1992). In the USA, cardiovascular disease only became common among African-Americans in the 1980s but has now reached the same level as in the white population (Walker, 1999). It can therefore be expected that all population groups will increasingly contribute to an increase of ischaemic heart disease in South Africa in the near future, highlighting a large demand for curative techniques in this country.

2.3.2 Economic Factors

During the past few years, several new devices for the treatment of ischaemic heart disease have been introduced. These techniques are mainly viewed in terms of the short- and long-term success and safety of coronary revascularisation. Increasingly, both the clinical and also the economic factors of the new devices have been studied since health care resources are limited and the number of patients is increasing.

It can be clearly shown that interventional techniques are more economic than surgical techniques. The total in-hospital costs are two to three times lower than for bypass (Cohen *et al.*, 1993). Looking at the interventional techniques only, coronary stenting has been reported as being more successful than PTCA alone but its hospital costs are significantly higher (Cohen *et al.*, 1993). Still, the more predictable immediate results and lower rates of restenosis compared to PTCA alone make it the technique of choice for the interventional cardiologist. A low restenosis rate can prevent the follow-up costs of a further procedure (Farshid *et al.*, 1999, Kelion *et al.*, 1999, Peterson *et al.*, 1999).

Examination of the catheterisation laboratory resource costs associated with each procedure demonstrates that the largest expense is the cost of the devices (PTCA balloons, catheters and stents) (Cohen *et al.*, 1993). Therefore the cost of a stenting procedure can be decreased by providing the interventional cardiologists with cheaper devices than the ones currently available in South Africa. In the case of this project, it is aimed to bring the current price of an imported stent implant of typically about R5 000 significantly down.

Cardiovascular disease has a severe impact on the South African economy. The estimated total cost in 1991 was between R4.135 billion and R5.035 billion, not including the cost of rehabilitation (Pestana *et al.*, 1996). This highlights not only the need for prevention strategies but also the need for finding ways of economically treating the disease.

The manufacture of medical equipment is in general more labour-intensive than that of other technical goods. This is due to the fact that the quality demand of these products must be extremely high (zero faults are tolerated). Labour-intensive quality control measures, mostly performed by highly trained personnel, are a prerequisite. Labour costs in South Africa are low compared to those of the western world, and thus locally manufactured goods can be offered at a price significantly lower than imported technical products of the same quality.

Every medical device that is sold, not only in South Africa but also elsewhere, has to be approved in the country of use. The cost for such approval is paid by the manufacturer and usually passed on to the customer. Also, the cost of product liability insurance, which is compulsory in some countries like the United States, may be part of the product price when the same product is offered in South Africa. The cost of international approval and insurance of the device are not necessary if it is only distributed locally. Also, the poor Rand exchange rate compared to other currencies such as the Dollar or the Deutsche Mark, means that imported goods are unnecessarily expensive.

2.4 Design Analysis of Currently Available Stents

Although the concept of intravascular stenting had already been proposed by Charles Dotter in 1969 (Dotter, 1969), it was not until 1986 that a stent was first implanted into a human coronary artery (Sigwart *et al.*, 1987). Several different stent design concepts have been developed since then. World wide, more than 50 different coronary stents are currently available. They are either a single tube with the wall perforated in a specific way or they are a structure of wires bent or interwoven in a tubular shape (Becker 1991; Eeckhout *et al.*, 1996; Katzen *et al.*, 1992; Marco, 1998; Serruys, 1998; Thomas, 1997). However, stents are generally described according to their method of deployment and are either self expanding or balloon expandable. Their design can broadly be divided into:

- self expanding wire mesh or single wire
- shape memory spiral coil
- balloon expandable single wire
- balloon expandable slotted tube

The common stents are metallic. This is because of the high radial strength required from the least bulk of material and the good radiopacity of metallic materials (Palmaz, 1992). Typically the outside diameters for coronary stents range between 1.0 and 1.5mm in the collapsed state and between 2.5 and 4.0mm in the expanded state. Wall thickness range between 0.06mm and 1.3mm in different designs.

2.4.1 Self Expanding Stents and Shape Memory Stents

A typical self expanding coronary stent of the wire mesh variety is the *Wallstent™* [2.9]. It is made out of stainless steel filaments that are woven into a tubular flexible configuration. The stent is compressed radially and mounted to the delivery catheter with a thin tubular membrane as a cover. At the target site the membrane is rolled back and the springloaded stent is allowed to expand (Figure 2.5). The *Wallstent™* was the first type of stent used in human coronary arteries (Sigwart *et al.*, 1987).

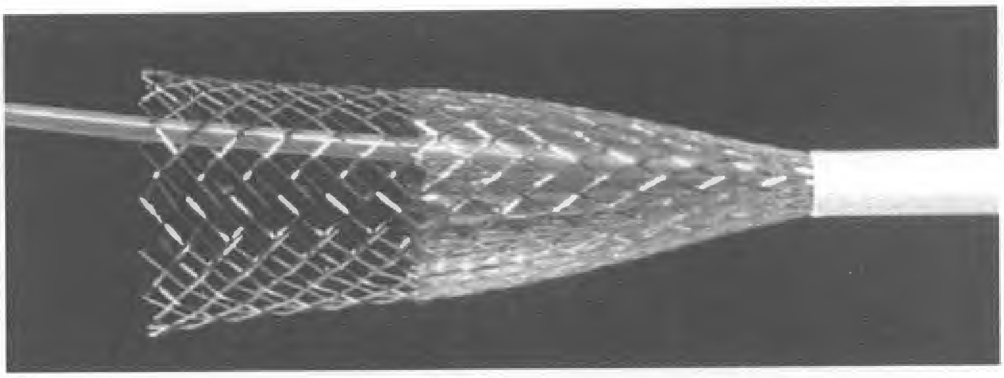


Figure 2.5 Self expanding coronary stents. The membrane overlying a Wallstent™ is withdrawn and the springloaded stent is released (image: Schneider).

[2.9] Schneider AG, Bülach, Switzerland

Self expanding stents made out of a single wire are also available, like the spiral-coil type *Cardiocoil™* [2.10]. This stent is wound onto the catheter to its lowest profile and is held and allowed to expand by a release mechanism inside the catheter.

Self expanding stents are springloaded and therefore need to be premounted on the delivery device, which means each self expanding stent design can only be used in combination with a specially designed catheter (Wright *et al.*, 1985).

Shape memory stents are made out of shape memory metal alloys (Nickel Titanium). They can be deformed for delivery when cooled down to temperatures far below body temperature (e.g., 0^0C in ice water). The stent will then "remember" its spiral coil shape when exposed to 37^0C inside the vessel. A highly specialised delivery device is necessary. This technique never reached the state of clinical application for coronary arteries because of technical problems in their handling (Zollikofer *et al.*, 1992).

2.4.2 Balloon Expandable Stents

These stents are either made out of a single wire or a mesh of wires (Palmaz *et al*, 1985), which is interwoven or bent into a tubular shape, or they are made out of a single tube that is slotted. Balloon expandable stents are either factory mounted or hand-crimped onto a PTCA balloon catheter in theater. Their deployed diameter is dictated by the diameter of the balloon used.

Examples for coronary stents of the wire variety include the *Cordis Crossflex*[2.11] stent and the *Strecker*[2.12] stent. Both are made out of a single tantalum wire structure forming a cylindrical tube. In the *Cordis Crossflex* stent the wire is bent in sinusoidal waves that are then wound to form a helical coil. The *Strecker* stent is formed by a wire that is knitted into a series of loosely connected loops forming a cylindrical tube. The *Gianturco-Roubin™*[2.13] and *Gianturco-Roubin II™* stents are examples for the use of a single stainless steel wire (Figure 2.6).

[2.10] InStent Ltd., Holon, Israel
[2.11] Cordis, a Johnson and Johnson Company, Warren, New Jersey, USA
[2.12] Medi- Tech, Watertown, Massachussets, USA
[2.13] Cook, Bloomington, Indiana, USA

The prototype slotted tube design stent is the *Palmaz-Schatz™*[2.14] stent, constructed of a stainless steel tube with rectangular slots in staggered rows. In the expanded stent the slots enlarge to diamond shaped openings (Figure 2.7).

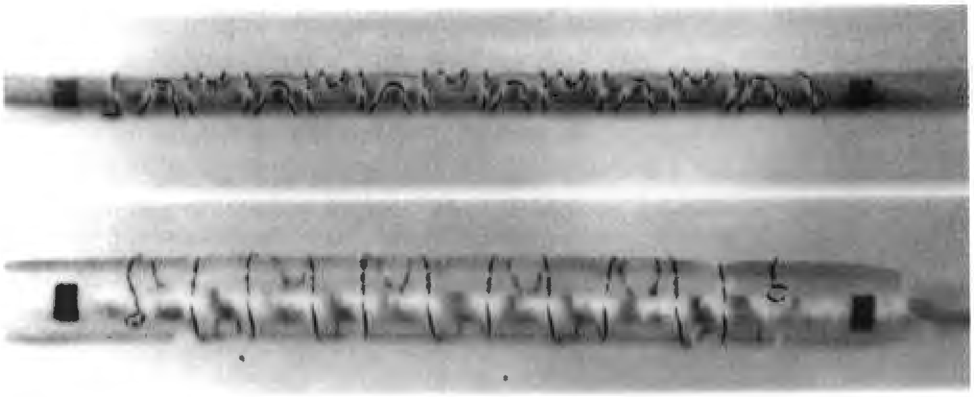


Figure 2.6 *Balloon expandable stents made out of wires. Gianturco-Roubin™ stent.*

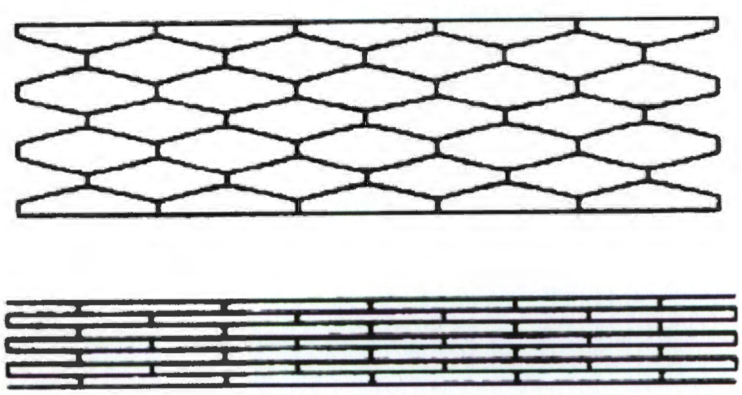


Figure 2.7 *The Palmaz-Schatz™ Stent represents the most basic slotted tube design (image: Johnson&Johnson).*

Derived from this simple design there are a number of advanced design variations available. The *Multilink Stent*[2.15.] is a stainless steel tube that is radially perforated with sinusoidal slots. Multiple links of material are left. When deployed, the pattern enlarges to an arrangement of multiple rings with multiple links. The *NIR Stent*[2.16], *JoStent*[2.17] and *DivYsio*[2.18] stent are further developments of this design idea. In all of them a sinusoidal- or zig-zag pattern of material

2.14 Johnson&Johnson Interventional Systems, Warren, New Jersey, USA
2.15 Guidant Corporation, Indianapolis
2.16 SCIMED Boston Scientific Corporation, France
2.17 JOMED International, Sweden

encompasses the circumference of the tube. Multiple rows of these sinusoidal rings are then connected by small links to form a continuos long tubular structure (Figure 2.8). These so-called 'corrugated ring' designs show improved longitudinal flexibility when compared to the basic slotted tube design.

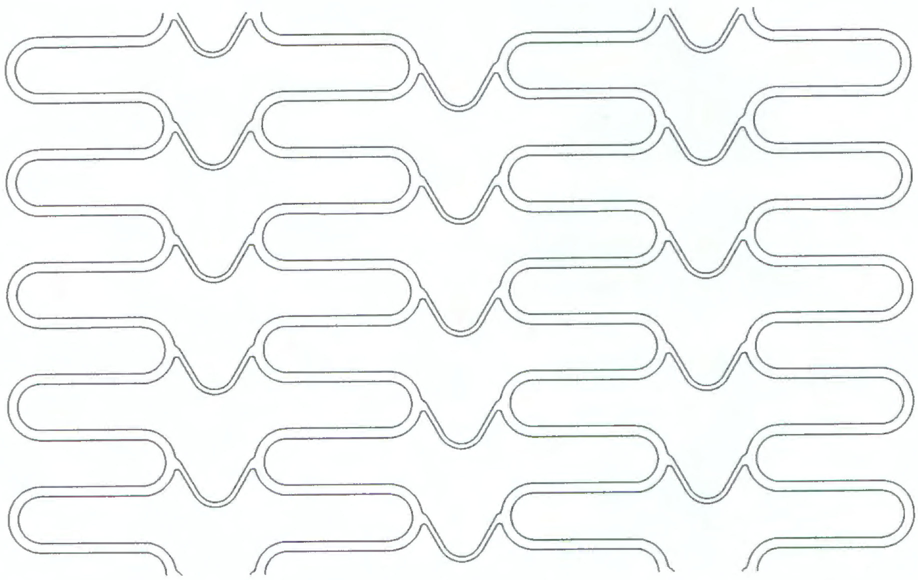


Figure 2.8 *Uncoiling image of the tube surface showing the principle of sinusoidal structures connected by multiple links.*

The above mentioned coronary stents represent only an overview of the basic design principles used for coronary stents, since development in this field is rapid and new stents are released frequently. Development mainly focuses on higher longitudinal flexibility and radipoacity of the stents but also on the reduction of thrombogenicity by surface treatments and coatings. There are also attempts to design stents out of biostable and biodegradable polymeric materials. This has not been successful yet and therefore metallic stents are still the only option for the use in treatment of coronary stenoses (Pepine *et al.*, 1996).

[2.18] Biocompatibles Ltd., Ireland

2.4.3 Discussion of Stent Design Types

The substantial differences in stent design and materials account for their varying radial compliance and radiopacity and also for a need of different delivery and deployment techniques. All design concepts of metallic stents successfully oppose the elastic recoil of vascular stenoses and provide internal vascular support. Still, the ideal stent does not exist. Available stents have advantages and disadvantages for specific uses (Agarval *et al.,* 1997; Becker *et al.*, 1991; Keane *et al.,* 1996).

Until recently the most commonly used and most extensively tested coronary stent was the *Plamaz-Schatz™* stent (Fischmann *et al.,* 1994; Karam, 1998; Moussa *et al.,* 1997; Schatz *et al.,* 1991; Serruys *et al.,* 1994). It was the coronary stent design concept of choice for the most frequent "straight forward lesions". It offers the simplest delivery method by any conventional PTCA balloon and a good radial compliance (Barth *et al.,* 1996; Keane *et al.,* 1996). An important fact contributing to its popularity is that it and the *Gianturco-Roubin™* stent were initially the only two designs that were approved by the Food and Drug Administration (FDA). For the first years of coronary stenting this made them the only designs that could be implanted in the USA. The major drawback of the *Palmaz-Schatz™* stent is its lack of longitudinal flexibility (Keane, 1996; Marco, 1998). The more recent 'corrugated ring' designs are still based on the original slotted tube principle but offer advantages in longitudinal flexibility over the *Palmaz-Schatz™* stent.

Several smaller trials have shown that the geometrical design of the stent has very little influence on the thrombogenicity of the stent and restenosis (Agarval *et al.,* 1997; Barth *et al.,* 1996; Chevalier *et al.,* 1997; Keane *et al.,* 1996; Moussa *et al.,* 1997). A higher restenosis rate was found in stent procedures using very flexible stents. This, however, was explained by the preferred use of flexible stents for tortuos vessels which are more prone to restenosis anyway (Rau, *et al.,* 1997).

A controversial issue is the necessary extent of vessel scaffolding provided. Extensive covering of the vessel wall seems to obtain better clinical results because it opposes herniation of tissue. Stents with a very open structure, on the other hand, are less likely to cover vessel side branches (Marco, 1998)

Thrombogenicity of the stent implant refers to the tendency of thrombus formation at the stent site. It is certainly one of the most important, frequently researched issues in stenting. In metallic stents, a very thin layer of metal oxide forms the interface between the implant and the host material. The sort of metal oxide and the surface structure as well as the amount of metal exposed to the bodies tissue seem to determine the thrombogenicity of the stent (Herrmann *et al.*, 1997). On the other hand, stents with a large metal surface support the vessel wall in a more effective and less traumatic way, cause less thrombogenic turbulence and prevent prolapse of arteriosclerotic plaque material into the vessel lumen (Fliedner *et al.*, 1997). Antithrombogenic coatings such as low-molecular-weight heparin and genetically engineered cells seem to reduce the thrombogenicity of metal, still the most favourable material (Herrmann *et al.*, 1997, Palmaz, 1993; Tepe *et al.*, 1996). Consequently one must assume that stents with a large exposed metal surface, coated with an antithrombogenic coating perform best in terms of restenosis and thrombogenicity. Meanwhile stents with different 'antitihrombogenic' coatings are being used, based on favourable initial results. Although there are no results available from clinical trials to prove the long-term advantage of such coatings (Bertrand *et al.*, 1998), their safety has been proven and they are used in current clinical trials (JOMED, 1997; Malik *et al.*, 1996).

A common problem of several stent designs, especially the ones with a thin walled stainless steel structure, is their poor radiopacity. This has been overcome in a number of stent designs by placing radiopaque gold markers at their ends, that show up in the angiogram and give a good idea of the stent position inside the vessel. The increasing image quality of digital angiography however, will decrease the need for such measures in the future.

2.5 Patent Research

The design concept of the new stent will be similar to an existing and accepted design on the market. It was therefore necessary to ensure that no existing patents were infringed when manufacturing and distributing a stent in

South Africa. A patent search relating to coronary and intravascular stents has been performed. This includes any South African patents, which could be infringed by a new coronary stent.

The DIALOG[2.19] database service is an electronic library with international access. It provides information about existing patents world-wide in the form of patent abstracts. This computer based search relies on the use of key words which must be present in the title or abstract of the patent. Therefore the possibility exists of not locating a patent which is relevant but has not been cross referenced correctly or in which relevant key words have been incorrectly spelt. Alternatively manual searches can be conducted but these ones also have a limited reliability. A computer based DIALOG database search with cross-checked results is considered to be more reliable than a purely manual search. Patent attorneys therefore use the latter one, as it is a reliable and cost effective survey (Spoor and Fisher 1999).

A database search was performed. All results were cross-checked with relevant abstracts in the DIALOG database and via the internet on the 'IBM patent server homepage' website[2.20] . Both provide bibliographic data of all claims of patents issued by the US Patent and Trademark Office (USPTO) from 1974 onwards. Also all patents world-wide registered since 1981 were considered. The key-words that formed the basis of the search were:

- intravascular
- stent
- intravascular stent
- surgical stent

More than 1000 different patents related to stenting were located. Most of them describe specific features of existing stent designs such as coatings with radiopaque or antithrombogenic materials or mechanisms for securement of the stent within the vessel lumen. Several polymeric stents have been patented as well as self-expanding designs in combination with delivery devices and crimping devices. No patents could be found in which the technique of stenting was claimed nor was the tubular geometry of the stents protected. A reason for this

[2.19] Knight-Ridder Information, Inc., California, USA
[2.20] http://www.patents.ibm.com

might be that the technique of stenting had already been described in the late 1960's (Dotter, 1969). It is therefore likely that registered patents affecting the method or the general principle of the implant would already have expired.

Several particular design features of existing balloon expandable slotted tube design varieties are protected by patents. They apply mainly in the United States and in Europe. In particular there are claims of specific geometrical designs having advantages for delivery or implantation of the stent. Improvements in the form of uniform deployment, longitudinal flexibility or structural openness were most frequently claimed.

In the course of the search only the following South African patents were located that relate to stent design:

81/7560	Low profile prosthetic xenograft heart valve
84/10032	Stent covering for tissue valves
94/0334	Clad composite stent
94/3522	Medical stent
95/10700	Endoluminal encapsulated stent and methods of manufacture and endoluminal delivery
96/3075	Drug release coated stent
96/7625	Drug release stent coating process
97/9900	Implantable fibers and medical articles
97/10342	Directional drug delivery stent and method of use

Only Patents 94/0334 and 94/3522 protect stent designs as such, the others describe drug release coated stents, stent grafts (fabric covered stents for the repair of aneurysms) or stents used to secure or scaffold heart valves. While patent 94/0334 describes a method of forming a stent from two sets of oppositely directed helical windings, patent 94/3522 protects a shape memory stent. Both are only relevant to very particular designs or manufacturing methods. Copies of both illustrated abstracts are enclosed in Appendix A.

Th other South African stent patents are only of relevance to a possible follow-up of this project. The stent to be designed and manufactured for this project will not infringe any existing South African Patents.

CHAPTER THREE

DEVELOPMENT OF THE CORONARY STENT

3.1 Defining the Design Concept

The first step in the development of a coronary stent was to evaluate which of the existing design concepts would be most suitable for manufacture and sale within South Africa. Therefore the four design ideas currently in use (section 2.4) were analysed by comparing their properties and characteristics. After the design properties of the stent to be designed had been laid down, the design concepts were judged for their ability to meet these criteria. The characteristics of a useful all-round stent are obtained from clinical trials and discussions with interventional cardiologists. A decision table was used to evaluate the most suitable design concept for the South African Market.

3.1.1 Required Characteristics

The list of required characteristics of an ideal coronary stent is long and varies with the specific purpose of use. Many of these characteristics are already met by most currently available metallic stents (Becker, 1991; Keane, 1995). However, certain characteristics of stent design concepts differ significantly amongst each other. In particular, their radial compliance, flexibility, radiopacity and their ease of delivery and deployment differ. Some challenges of stent design have been identified but not solved, at least not without accepting drawbacks in other important characteristics. These include the possibility of removing of a fully deployed and placed stent and the thrombogenicity of the stent material. This, however, would only be an issue after the first prototypes have been successfully manufactured and mechanically tested and is not part of the current project.

The aim of this project was to design a multiple purpose coronary stent that can be used in the majority of cases. Thus it must be suitable as a substitute to the stent currently used for the so-called "straight forward lesions" in interventional centres throughout South Africa. Its properties therefore need to be similar to those of the already well accepted and proven stent designs, the difference being that it is offered at a competitive price (Section 2.3.2).

Five main criteria were used in the process of deciding what stent design concept to choose for development. Not all the criteria are of equal importance for the choice of a suitable solution. Therefore they were valued with weighting factors W ($W \in \{1, 2, 3\}$), with 3 representing the most important criterion. Each factor was given in square brackets after the explanation of the criterion. Criteria without a factor (Criteria I & II) were found to be of such high importance that, if a particular design concept did not fulfil them, it was removed from further consideration. The most important characteristics of the coronary stent for the South African market were found to be:

I. Manufacturability

The stent shall be manufactured by using the locally available manufacturing equipment. To keep production costs low and ensure a constant quality standard, the production must be mainly automated. In the case of this project there are numerically controlled lathes and milling machines available. There is also access to a numerically controlled spark erosion machine and a wire erosion machine. Investment in other manufacturing techniques must be avoided to keep the costs low.

II. Use of an existing delivery system

The stent shall be delivered and deployed by using a conventional PTCA catheter. The development and manufacture of a special delivery system (balloon, etc.,) for the coronary stent would increase the manufacturing costs unnecessarily.

III. Radial strength

The main purpose of a stent is to provide vessel patency by uniform circumferential scaffolding. It must therefore have radial strength and a reasonably dense structure to resist the pressure applied by the muscular arterial walls (section 2.1). The stent placement is irreversible and failure of sufficient deployment and radial compliance of the stent may result in thrombosis. On the other hand the stent must not impose too high a work load on the balloon so as to avoid exceeding its pressure limits. It was found that the pressure required to deploy currently available stents is at the low end of the pressure range of a typical PTCA balloon and does not add to balloon stress at high pressures (Palmaz *et al.*, 1998). The radial strength of several different stent designs has been evaluated in experiments (Agraval *et al.*, 1992; Fallone *et al.*, 1988; Keane, 1995). The importance of this criterion is weighted [W=3].

IV. Longitudinal Flexibility

The stent has to be manoeuvred around tight corners and small radii along the guide wire to reach distal lesions. For this reason a good longitudinal flexibility is desirable and its importance is given a weighting of [W=2].

V. Radiopacity

For visibility under angiographic imaging during the procedure and for control purposes after the intervention, the stent needs to be radiopaque. The radiopacity is determined by the wall thickness and density of the stent structure and by the material used. In case of low radiopacity, the stent can be coated with highly radiopaque material, therefore the criterion is less important for the stent design than the previous ones and is given a weighting of [W=1].

There are four different design concepts for metallic coronary stents currently in clinical use (section 2.4):

A. self expanding wire mesh
B. self expanding single wire
C. balloon expandable single wire
D. balloon expandable slotted tube

It is necessary to evaluate how well each of the four concepts can meet the design characteristics I. to V. described above. Each of the designs is judged for its ability to meet a specific requirement. The suitability S_n of the designs is graded by values X_n ($X \in \{1, 2, 3\}$ and $n \in \{A, B, C, D\}$), with 3 representing the best suitability to a specific requirement. Again the values X_n are given in square brackets. If a design meets requirements I or II, it is assigned [yes], if does not it is assigned [no].

A. Self expanding wire mesh

The stents can be manufactured by bending and weaving wires into a specific pattern. In mass production this can only be accomplished in an automated way by using an automated wire bending machine. These machines were not immediately available for this project, therefore wire mesh stents are not suitable for easy manufacturing [no].

Self expanding stents are springloaded when they are restricted to their lowest profile. They have to be premounted to a particular delivery device that has a specialised release mechanism. Design and manufacturing of a special delivery catheter is not an option for this project, springloaded stents are therefore not suitable [no].

The radial compliance of the available self expanding *Wallstent* is described as being significantly lower when compared to other stents (Keane, 1996). The wire structures seem to have low radial strength and only qualify for grade [X=1].

The loose structure of wire stents accounts for their excellent longitudinal flexibility, hence wire mesh stents reach the highest grade of [3] for potential longitudinal flexibility.

The wires are typically very thin (e.g., *Wallstent:* filament diameter of 0.08 - 0.1mm). These stents therefore typically show up weakly on angiograms (Keane, 1996) and their radiopacity is graded to be [X=1]

B. Self expanding single wire

These stents can be manufactured by bending one wire into a specific pattern. Again, since there was no access to an automated wire bending machine for this project and single wire stents are found to be not suitable for easy manufacturing [no].

Like the self expanding wire mesh stents listed above, this design concept has to be premounted onto a special delivery device and for this reason is not suitable for this project [no].

There is no test data available on the radial compliance of a self expanding single wire stent. However, in a 1996 trial that compared the radial compliance of different stent designs, it was stated that "The findings of our studies were consistent with the expectations from the strut thickness and configuration and metallic composition of each stent design." (Keane, 1996). Since the single wire is about two times thicker than the filaments of the *Wallstent*™ (e.g., *InStent*™*:* wire diameter of 0.2mm), it can be expected to have a higher radial strength than typical wire mesh stents and therefore reaches grade [X=2].

Similar to the self expanding wire mesh stents above, wire structures show excellent longitudinal flexibility and this design concept therefore is assigned the highest grade of [X=3]

The relatively thick wire (as opposed to the thin filaments of the *Wallstent*™) gives it a better radiopacity than the wire mesh and the single wire design reaches a grade of [X=2] for potential radiopacity.

C. Balloon expandable single wire

As with design concepts A. and B., these stents need to be manufactured by bending a wire into a specific pattern which, as described above, cannot currently be automated in this case and was found to be a non suitable design concept from a manufacturing point of view [no].

Stents of this design can be mounted onto a conventional PTCA balloon by simply crimping them on. They therefore qualify as suitable for this project [yes].

The radial compliance of the available balloon expandable single wire design stents is high (Keane, 1996). Simply choosing a larger wire diameter can even increase it. For these reasons it is a suitable design concept for achieving radial strength and is given the highest grade of [X=3].

Again, being a wire structure, this design concept shows very good longitudinal flexibility and is given the highest grade of [X=3].

Stents made out of Tantalum wire show excellent radiopacity (Keane, 1996), the general radiopacity of balloon expandable stainless steel wire stents can also be improved easily by choosing a thicker wire. It is therefore considered to be a suitable design to achieve high radiopacity. [X=3]

D. Balloon expandable slotted tube

These stents can be manufactured by perforating a stainless steel tube by automated spark erosion. The tubes can either be purchased with the correct dimensions or manufactured by using a numerically controlled lathe. This utilises available manufacturing techniques [yes].

Like the balloon expandable single wire design, these stents can be mounted onto a conventional PTCA balloon simply by crimping them on by hand. This is therefore an optional design concept for this project [yes].

The radial compliance of available balloon-expandable stents made from slotted tube is described as being high (Keane, 1996). It can also be increased by simply choosing a tube with a slightly thicker wall. The design variety is therefore found to have potential for high radial strength and gets assigned a grade of [X=3].

The "classic" stent of this design variety, the *Palmaz-Schatz* stent, has poor longitudinal flexibility (Keane, 1996). The longitudinal flexibility is largely dependent on the design of the struts and slots in the tube wall. The latest available designs are significantly more flexible than their predecessors. The slotted designs only reach a grade of [X=2] having a potentially lower longitudinal flexibility than wire structures.

The radiopacity of plain slotted tube stents with their typical wall thickness of about 0.1mm is described as being poor (Keane, 1996) and the design variety is given a low grade [X=1].

3.1.2 Choice of the Most Suitable Design Concept

The outcome of the above discussion was summarised in a decision selection table below (Table 3.1). Each specific suitability value X_n was multiplied by the weighting factor W for the requirement (Equation 3.1). The results S_n were then added up and the highest sum T_n represents the design best suited to meet the five requirements (Equation 3.2).

$$S_n = W * X_n \tag{3.1}$$

$$T_n = \sum S_n \tag{3.2}$$

design concept		X_A	X_B	X_C	X_D
requirement	weighting factor W				
manufacturing		no	no	no	yes
delivery system		no	no	yes	yes
radial compliance	3	1	2	3	3
flexibility	2	3	3	3	2
radiopacity	1	1	2	3	1
Total T_n		10	14	18	**14**

Table 3.1 Decision table for selecting the most suitable design concept.

Although they show clear advantages, especially in terms of their longitudinal flexibility, the design concept of self expanding stents (A and B) is unsuitable to be manufactured for the South African market. They would have to be factory-mounted onto a delivery device, when springloaded to their lowest profile. This would require the design and production of special delivery catheters with release mechanisms for these stents.

The design idea of balloon expandable single wire stents (C) is most suitable according to the criteria described above. Good radial compliance can be achieved by using a strong wire, the longitudinal flexibility is excellent and the use of tantalum wires gives very good radiopacity. However, for all the stent design concepts based on a wire structure, there are no automated facilities available for the current project to manufacture them cost effectively. Therefore design concept C is unsuitable for this project.

The design concept chosen to be suitable for manufacturing and sale in South Africa is the balloon expandable slotted tube design (D). The results of Table 3.1 show that although it does not meet the requirements best compared to the other three design concepts, it is the only one that can be manufactured in an automated way with the manufacturing equipment available for this project. A major drawback of slotted tube designs is their typically poor radiopacity. This, however, can be overcome by plating the stent surface with radiopaque material (sections 2.4 and 2.5). It would improve the grade for the criterion of radiopacity from 1 to 3 and the total sum T_D to 16.

The stent design chosen is also the most popular concept world-wide and is used in the majority of the cases treating the so called "straight forward lesions" (section 2.4).

3.2 Design of the Coronary Stent

3.2.1 Material

The coronary stents currently in use are made out of metal. The typical properties of metallic materials in terms of toughness, hardness and plastic deformability allow a high expansion ratio and a high radial compliance of the stent structure after deformation. The most commonly used alloys for vascular implants including stents are the medical grade 300-series stainless steels (Palmaz *et al.,* 1998). Their high chromium content makes them extremely corrosion resistant and biologically inert. For this project it is essential to use a material of known biocompatibility and thrombogenicity, thereby avoiding the need to test the materials (section 2.4).

The material used for most of the currently available coronary stents of the balloon expandable slotted tube design type is surgical grade stainless steel 316L (UNS Number S 31603/ DIN Number 1.4435). It is an austenitic stainless steel with a face centred cubic crystal structure. Stainless steels of this structure possess excellent ductility, formability and toughness. They can be substantially hardened by cold work. Stainless steel 316L is widely used in the medical implant industry because of its extremely high corrosion resistance and its purity (ASM International, 1996; Wegst, 1989). It has proven to be biologically. It can therefore be safely assumed that its biocompatibility and material properties (Table 3.2) are appropriate for the stent to be designed in this project.

Elongation	40%
0.2% yield stress	190 MPa
Tensile strength	490 Mpa
Young's Modulus	190 Gpa
33% elongation @ 679MPa	

Table 3.2
Material properties of 316L stainless steel.

3.2.2 Manufacturing Method

To manufacture a coronary stent with a balloon expandable slotted tube design, the wall of a tube must be perforated in a specific way. The perforation of the tube wall occurs in a repetitive pattern of similarly shaped openings arranged around the circumference of the tube. When deploying the stent, the openings widen, increasing the circumference of the tube. A simple example is the "classic" *Palmaz-Schatz* stent described earlier (Figure 2.7).

Almost all stents with a slotted tube design are manufactured by cutting slots into a tube with a laser beam. The specialised laser cutting equipment is available but very expensive and would increase the cost of a locally manufactured coronary stent by magnitudes. The challenge for this project lies in finding an economic way of manufacturing a coronary stent by using the equipment currently available. Because of the flimsy structure of the stent, machining by mechanical cutting does not seem to be a feasible way of manufacturing. With this method, the tube would have to be clamped tightly to the machine, which would deform its structure. Also, the resulting forces during cutting the thin tube would probably destroy it.

Perforating the tube wall using thermal processes reduces the forces applied to the workpiece to almost zero. These processes require exact positioning of the workpiece only with no large clamping forces being necessary to hold it in place.

A suitable way for removing material (stock removal) is the spark erosion technique. For this project there was access to a numerically controlled spark erosion machine. Stock removal in spark erosion machining is performed by direct conversion of electrical energy into heat. One electrode, acting as tool, removes material from the workpiece, which serves as the second electrode. As a result, the material melts and is removed.

A pulsating electrical voltage forms an electrostatic field between the electrodes. The electrodes do not touch each other and are separated by an insulating dielectric fluid. At the maximum pulse voltage, the electrical field discharges. At the point where the tool electrode and the workpiece are closest, current flows. This forms a widening discharge channel by forming gas bubbles restricted by the surrounding, highly viscous dielectric fluid. This restriction is responsible for a very high energy density inside the discharge channel. Temperatures of between 8 000 and 12 000^{0}C cause the material of both the electrode and to a greater extend the workpiece to melt. At the end of the pulse, the current and with it the heat supply is interrupted. The molten material is ejected due to combined thermal, mechanical, electrical and magnetic forces.

The tool electrode is feed driven and leaves an impression or an opening the negative of its own shape in the surface of the workpiece (Figure 3.1). All electrically conductive materials can be machined by spark erosion technology irrespective of their particular mechanical properties.

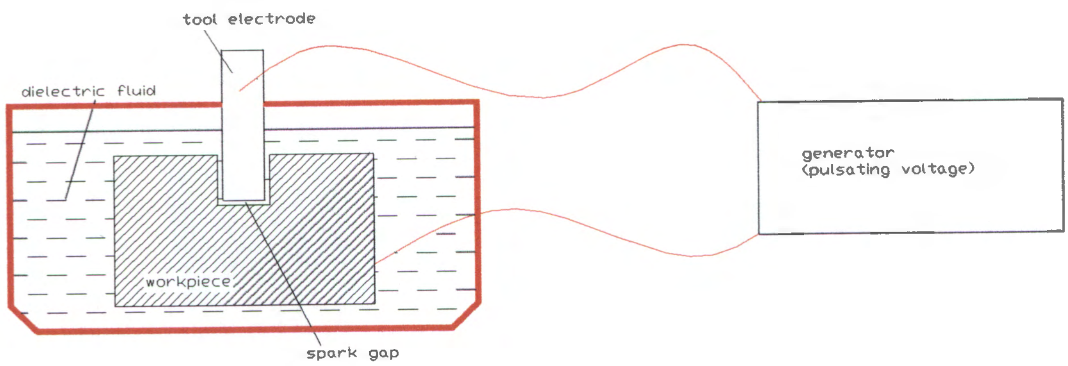


Figure 3.1 Principle of a spark erosion machine.

Spark erosion allows the perforation of the thin tube wall with openings of almost any shape desired as long as the negative shape of the electrode can be manufactured. Commonly copper electrodes are used as tools for the spark erosion process. They are cut out of a solid copper plate by wire erosion.

Similar to spark erosion, in wire erosion stock removal is performed by converting electrical energy into heat. The tool electrode in this case is a wire that is fed through the material similar to a jigsaw and "cuts out" a prismatic shape. The path of the wire through the material is usually numerically controlled. In this manner almost any desired shape of prism can be programmed and cut out of solid plates. Limitations are given by the diameter of the wire, which makes it impossible to manufacture sharp corners (e.g., the smallest inside radius to be produced with a 0.3mm diameter wire will theoretically be 0.15mm).

3.2.3 Stent Design

Balloon-expandable stents of the slotted tube variety are made out of multiple, radially expandable rings that are connected by links to form a long, tubelike structure (section 2.4) (Figure 2.10). This ring of sinusoidal structures provides the main function of a coronary stent, namely the radial expansion. The stiffness of the links between the rings is responsible for the longitudinal flexibility of the stent structure (Figure 3.2).

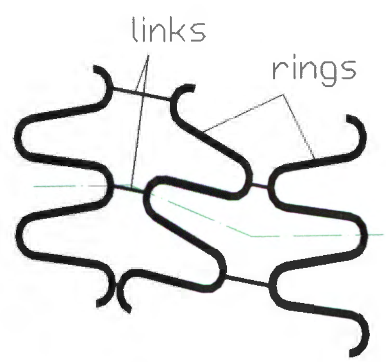


Figure 3.2 Uncoiling image of the tube surface showing the principle of sinusoidal structures connected by multiple links.

Thus it seems reasonable to design a stent with a strong expandable ring structure for good radial compliance, connected by more compliant links to provide good longitudinal flexibility. The links need to have a geometry that controls the way they deform (e.g., they should not bulge out radially when they become compressed). They must also be able to stretch out when they get expanded (Figure 3.3).

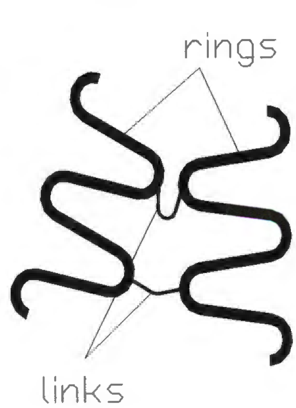


Figure 3.3 The geometry of the links ensures a controlled deformation.

The geometrical features described are included in the latest developments of stents with a balloon-expandable slotted tube design. Examples are the *NIR* stent and the *JoStent™* (Figure 3.4). There is no comparative data available at this stage but discussions with interventional cardiologists confirm that this latest design seems to meet the requirements best in terms of radial compliance combined with longitudinal flexibility.

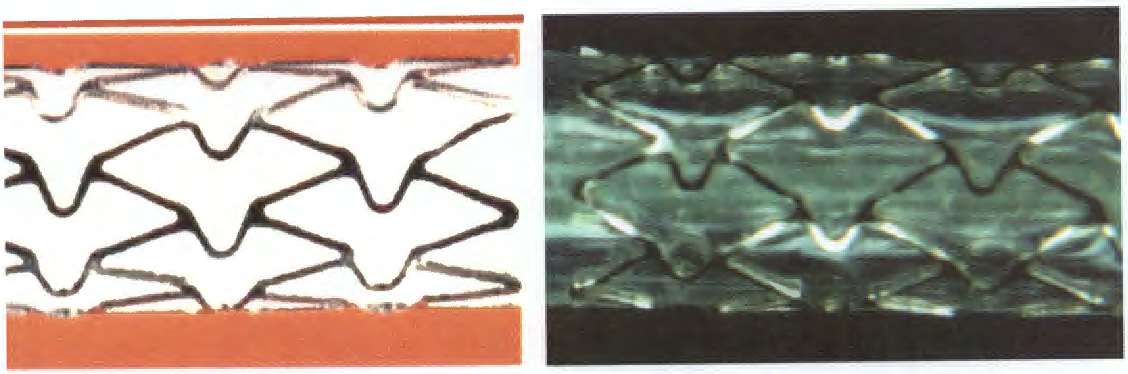


Figure 3.4 Structures of the JoStent™ (left)(picture: Jomed) and the NIR Stent (right). They show the typical design features of the new generation slotted tube design stent with multiple sinusoidal rings connected by multiple rings.

Basic design Parameters of the Prototypes

Stent Size

Coronary stents are available in a variety of sizes. In the design of the first stent prototypes, the focus was on one common stent size. After successfully producing the first prototypes, the design can be adapted to manufacture different sizes. Three stent diameters of are relevant:

1. the diameter at which it is manufactured
2. the diameter to which it can be crimped when mounted onto the PTCA balloon, the crimped profile P.
3. the maximum diameter it reaches when it gets deployed by the PTCA balloon

For the purpose of prototyping and testing the new design, stents were manufactured to fit PTCA balloons having a nominal (deployed) diameter of 3.5mm. These balloons typically have a deflated profile of ≥0.8mm providing for a crimped outside diameter P of a stent, with 0.1mm wall-thickness, of about 1mm.

The length of the stent L_0 should be between 8 and 10mm. It is influenced by the number of corrugated rings c along the longitudinal stent axis, their individual length L and the length of the individual links l.

$$L_0 = c * L + (c-1) * l[mm] \tag{3.3}$$

Typically the wall-thickness of stents available in the slotted tube design is 0.07 to 0.1mm, the width of the struts of the sinusoidal rings is approximately 0.1mm (Table 3.3).

Stent Geometry

Geometrical dimensions influence the properties of the stent. The seven most important properties for the slotted tube design were identified as being:

1. Radial compliance. The main purpose of a stent is to expand the lumen and to provide patency for the vessel it is inserted into.
2. Longitudinal flexibility. This ensures that the stent can be manoeuvred into tortuous vessels and therefore be placed in distal lesions.
3. Radiopacity. Determined by the used material and the density of the stent (struts to gaps ratio, metal content). It is influenced by the dimensions and design of the struts and the presence of radiopaque coatings or markers.
4. Side branch access. Struts of the stent can overly side branches of the treated artery and decrease or block off blood flow. A very open structure with thin struts decreases the possibility of struts overlying a side branch.
5. Minimal strut induced injury: determined mainly by the geometrical shape of the cross sections of the struts, like wide struts with smooth edges.
6. Low profile P after mounting (crimped profile): determined by the number n of cells and radii fitted around the circumference and their dimension R in the sinusoidal folded ring structure (Equation 3.2), assuming that R stays constant during crimping.

$$P = \frac{\pi}{n * R}[mm] \tag{3.4}$$

Not necessarily influencing the properties of the stent but important for rapid acceptance of the stent by cardiologists in South Africa is proximity to a well accepted geometrical shape of a proven design.

The six main design parameters for the stent were identified as follows. By changing each of them separately while keeping the others constant, the properties of the whole stent can be influenced, and the influence of each parameter can be analysed (Table 3.3). The increase of dimensions L, W, Y, R and T (Figure 3.5) influences the properties listed in the column on the left-hand side of Table 3.3. positively ($\Uparrow$) or negatively ($\Downarrow$).

1. The corrugated ring structure forms the supporting scaffolding for radial vessel support. A large dimension L (long struts mean long levers) makes it easier to deform the radius R, hence reduces the stent's radial strength. A long, rigid ring made op out of short levers has a negative influence on the longitudinal flexibility. It doesn't necessarily have any influence on the metal content of the stent and its radiopacity. The size of the openings increases with the length of the rings and with it the side branch access. There are no distinctive influences on strut-induced injury and the crimped profile of the stent. However, for 12 of struts being to encompass the circumference of a fully deployed stent the sum of their lengths must exceed the curcumference of 4.0mm (Equation 3.4).

$$\sum 12 * L > 4.0mm * \pi \qquad (3.5)$$

   In this case it means the levers must be at least 1.05mm long.

2. The number of cells n around the circumference has probably little or no influence on the radial compliance and no influence on the longitudinal flexibility of the stent. There is an influence on its radiopacity, since many cells also contain many struts resulting in a structure with high density (metal content). Many cells and with it many struts have a negative impact on the size of the openings and the side branch access but a positive influence on the safety of the stents in terms of less strut induced injuries with more struts supporting the vessel wall. The lowest crimped profile will

be larger since there are more cells and struts to be packed around the circumference when crimped (Equation 3.2).

3. Increasing the width of the struts W increases the second moment of inertia[3.1] I in the direction of the main deformation (Figure 3.5) and therefore the radial strength significantly since the width W influences the moment of inertia I as a factor to the power of three (Equation 3.3). It also increases the metal content and radiopacity of the stent.

$$I = \frac{T * W^3}{12} \left[m^4\right] \qquad (3.6)$$

(with T being the wall-thickness)

The corrugated rings are a rigid unit when the stent is bent longitudinally. Therefore dimension W has no influence on the longitudinal flexibility. It has little effect on the side branch access and the crimped profile of the stent. Wider struts greatlyly improve the vessel support and the stent safety in terms of strut induced injury.

4. The width of the links Y influences the longitudinal flexibility of the stent. Wider linkeage struts are more rigid but also less traumatic and increase the total metal content, hence the radiopacity of the implant.
5. Besides the number of cells n around the circumference, an increased size of the radius R negatively influences the profile the stent can be crimped to (Equation 3.2).
6. The wall thickness T generally influences the rigidity of the stent structure in every direction although not to the same extent as the strut width W (Equation 3.3). A thick wall will improve radiopacity and add to the crimped stent profile.

Also see section 2.4

Based on the findings in Table 3.3 and in accordance with the common dimensions in existing corrugated ring slotted tube designs, the design parameters for the stent were chosen (Table 3.4).

[3.1] The second moment of inertia is a measure for resistance of a longitudinal structure to bending deformation.

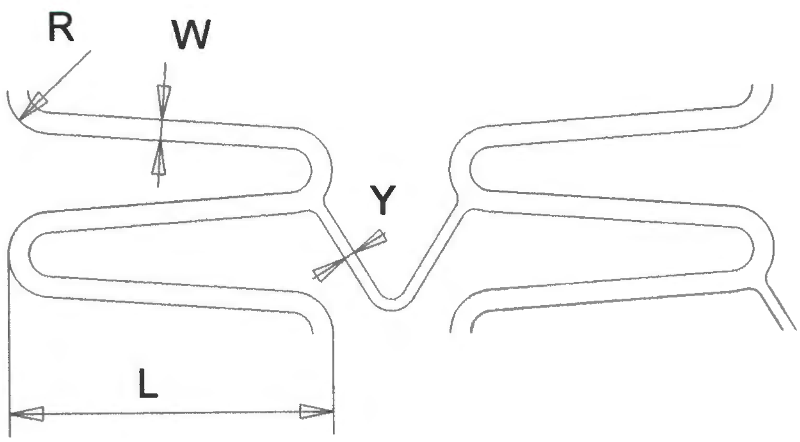


Figure 3.5 Basic design parameters of the stent.

To design a stent of between 8 and 10mm in length and in accordance with the typical ring lengths L of existing designs, it seems reasonable to choose 4 rings along the length with a ring length of +/-2mm.

The spark erosion machine is fitted with an indexing head that allows it to rotate the tube about its longitudinal axis in 30^0 steps. Therefore 6 openings around the circumference of the tube are conveniently chosen as a design parameter.

The strut widths W in most of the existing designs varies between 0.1 and 0.09mm. For the ring struts of the stent to be designed, a width of 0.1mm was chosen to ensure high radiopacity and security in terms of strut induced vessel injury.

Narrow links (width Y) of 0.05mm width result in a stent with good longitudinal flexibility. The larger and more rigid ring struts provide the main vessel support, therefore the expected vessel injury potential caused by the links is estimated to be low.

The radii R are designed to fit a circumference of a 6 cell stent crimped to 0.8mm. six radii around a circumference of 2.5mm: R<0.4mm.

Commonly the wall thickness of stents of the slotted tube design variety is determined by the equal to the strut width W and is therefore chosen to be 0.1mm.

Increase of	Length of ring structure L	NR. of cells n	Width of struts W	Width of links Y	Size of radius R	Wall thickness T
Radial compliance	⇓	-	⇑	-	-	⇑
Longitudinal flexibility	⇓	-	-	⇑	-	⇓
Radiopacity	-	⇑	⇑	-	-	⇑
Side branch access	⇑	-	-	-	-	-
Strut induced injury	-	⇑	⇑	⇑	-	-
Low crimped profile P	-	⇓	-	-	⇓	⇓

Table 3.3 Influence of design parameters on the stent properties.

Manufacturing diameter	1.8mm o.d.
crimped on diameter	1.0mm o.d.
deployed diameter	3.5mm i.d.
stent length	8mm - 10mm
corrugated ring length L	+/-2mm
number of cells n	n = 6 every 60^0 around the circumference
strut width W	0.1mm
Link width Y	0.05mm
wall thickness T	0.1mm

Table 3.4 Design parameters for the stent.

Stent Surface

A smooth stent surface without sharp edges or burrs is desirable. Besides the obvious advantages in terms of haemodynamic turbulence this will avoid injuries to the vessel and damage to the thin walled PTCA balloon. Also, it has been shown that stents treated by electrochemical polishing decrease thrombogenicity after implantation because of their smooth surface (De Scheerder *et al.*, 1997; Palmaz *et al.*, 1998). Electropolishing in metals provides a combination of a smooth surface finish and deburring of edges by removing a small amount of surface material in metals. It also removes most of the trace elements from the metal surface leaving a high concentration of chromium, which rapidly turns into chromium oxide. This layer of only a few nanometers seals the bulk material and its supposedly thrombogenic trace elements off from blood contact, stabilises the surface and prevents further oxidation. Therefore a layer of chromium oxide provides the actual interface with the blood after implantation (Palmaz *et al.,* 1998). Stainless steel materials have been electropolished with good results (ASM, 1980).

Initial Prototype

To evaluate the feasibility of the general design and manufacturing principle a tube with an outside diameter of 2.3mm and a wall thickness of 0.1mm was perforated with the desired pattern. A rather conservative design pattern similar to the ones used in the *JoStent*™ and *NIR* stent was roughly fitted to the surface of the tube. Suitable copper electrodes were designed for the spark erosion (Figure 3.6 and Appendix B2.1). This made it possible to determine the geometrical outcome in terms of sparking gaps and achieved tolerances. A more specific electrode design for a second prototype was subsequently based on the geometrical outcome of the first cutting.

To compensate for the wedge shaped geometry of the cross section of the stent struts caused by intersection of the electrode profile with the curved tube surface, all calculations and drawings were based on the middle layer of the tube wall (Figure 4.7). In the case of this first prototypes this was a tube with 2.2mm diameter. The circumference of a cylinder of 2.2mm diameter is 6.91mm, which allows the opening to be repeated six times every 1.15mm around the circumference. The length of the chosen pattern is 8.7mm and lies within the desired dimensions. The strut width of the sinusoidal structure was chosen to be approximately 0.1mm similar to already existing designs. The links are considerably narrower to provide longitudinal flexibility as described earlier in section 3.2.3. In this case they are chosen to be 0.05mm. For the first prototype the electrodes were cut to size without taking a sparking gap into consideration (Figure 3.2 and Appendix B1).

The prototype was spark eroded, this will be described in Chapter 4, using the manufactured tools and appliances described in section 3.2.4.

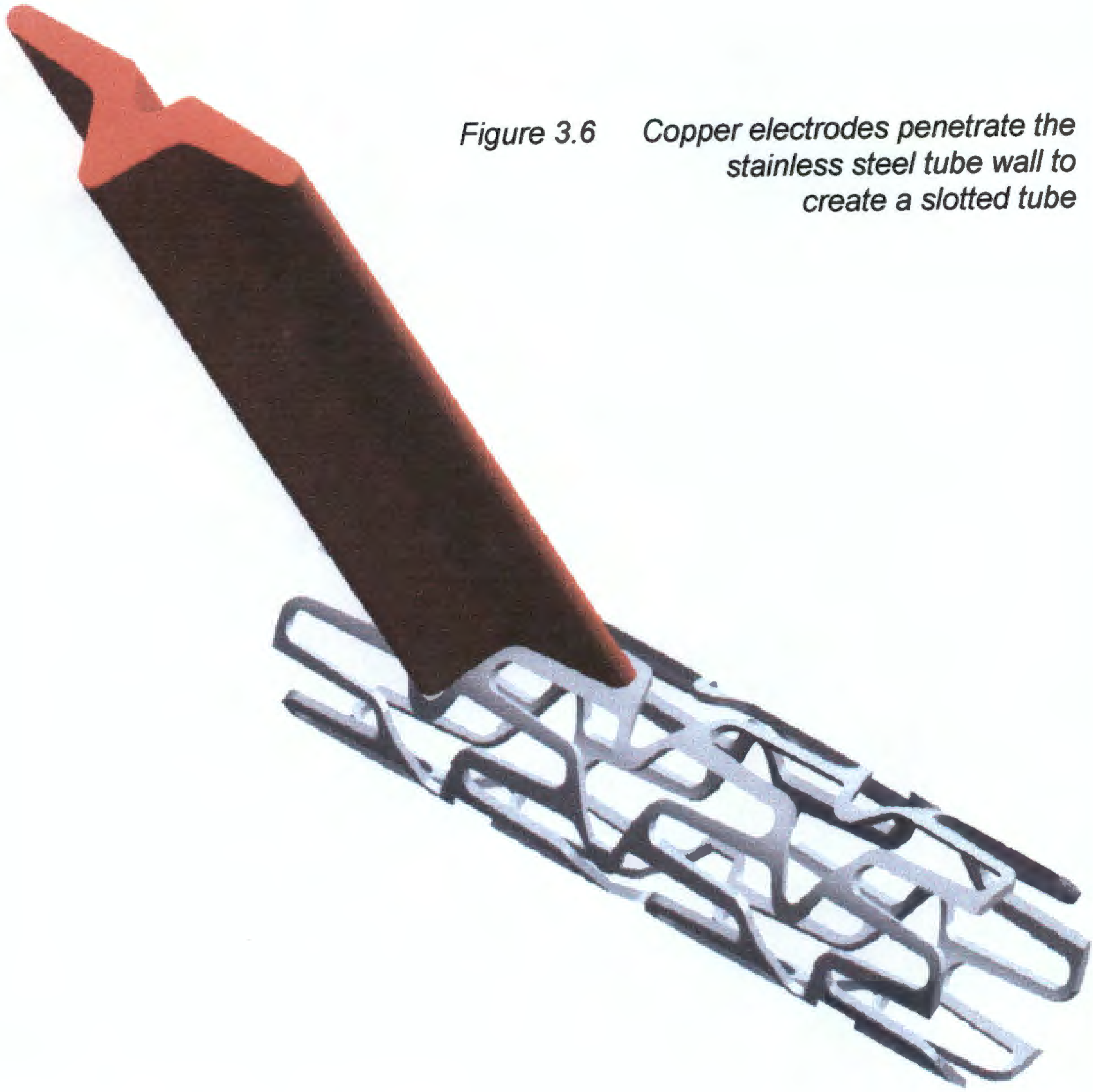


Figure 3.6 *Copper electrodes penetrate the stainless steel tube wall to create a slotted tube*

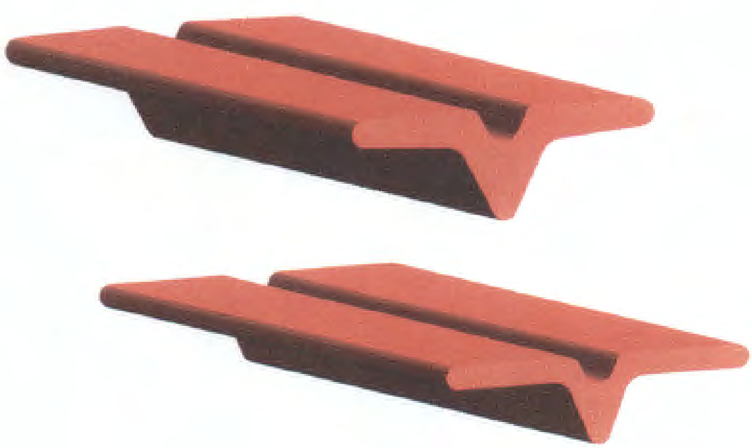


Figure 3.7
Electrode shape for prototype 1 (top) and 2 (bottom).

Final Prototype

The final prototype was designed with the knowledge of the geometrical outcome of the manufacturing process. The design of the electrodes for the final prototype was therefore adjusted to the (reduced) final tube diameter of 1.8mm (1.7mm effective diameter of the middle layer) (Figure 3.7 and Appendix B2.1). The wall thickness was kept at 0.1mm. A spark gap of 0.025mm was taken into consideration (Appendix B1).

3.2.4 Tools and Appliances

Electrodes

The electrode tools for the spark erosion of the openings in the tube wall are manufactured by wire erosion, described in section 3.2.2. CAD drawings of the electrodes were drawn for both prototypes and exported as .dxf files to be read directly into the control of the wire erosion machine (Appendix B2.1). A set of 5 electrodes of each prototype was cut to be used in the electrode holder for the spark erosion process.

Electrode Holder

To hold a row of 5 aligned and positioned electrodes, an electrode holder was designed. It consists of a rod with notches to take up and position the electrodes and a simple clamping device (Appendix B2.2 and Figure 3.8).

Support Pin

The cut stent has a very flimsy structure and it is therefore difficult to cut it off the remaining tube. For this reason the tube is cut to length before spark erosion of the openings and press-fitted on to a pin (Figure 3.19). The distal end of the pin is supported by a tapered tip (Appendix B2.3).

The pin was designed to allow for the tube to be pushed against a shoulder on the pin. The row of electrodes can then be positioned correctly relative to the tube by touching a second shoulder (Figure 3.10). The pin also forms a core inside the tube, stabilising the structure and helping to keep tight tolerances.

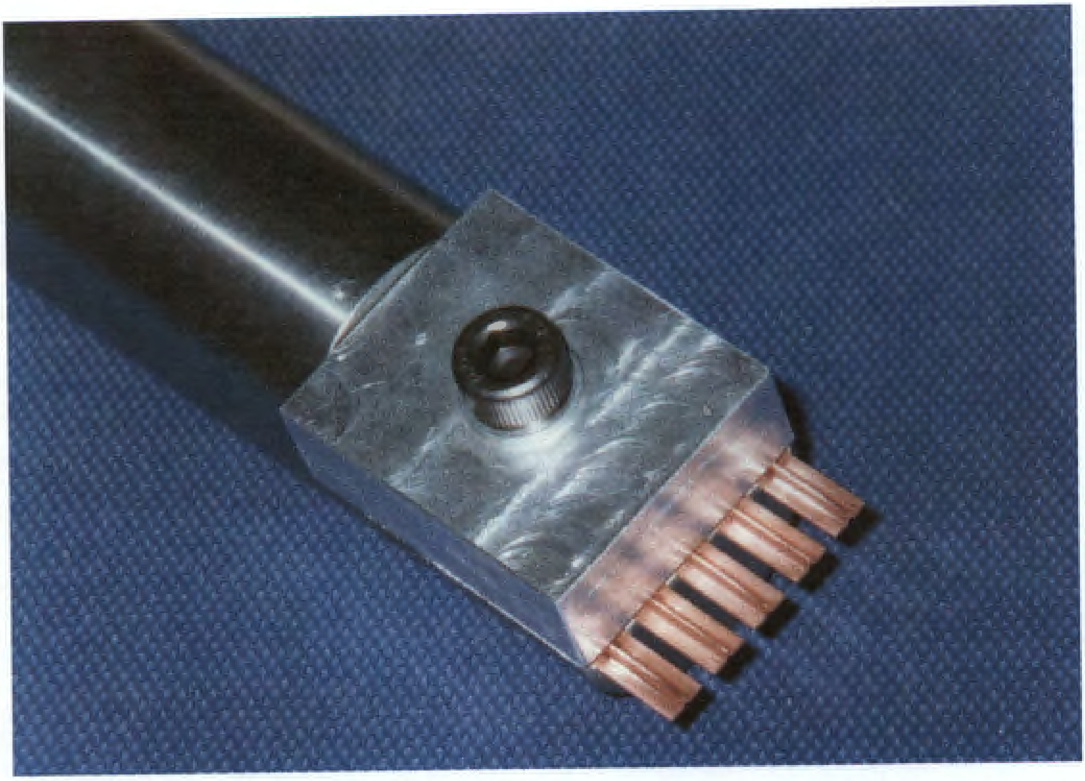


Figure 3.8 *Electrode holder with a set of tool electrodes.*

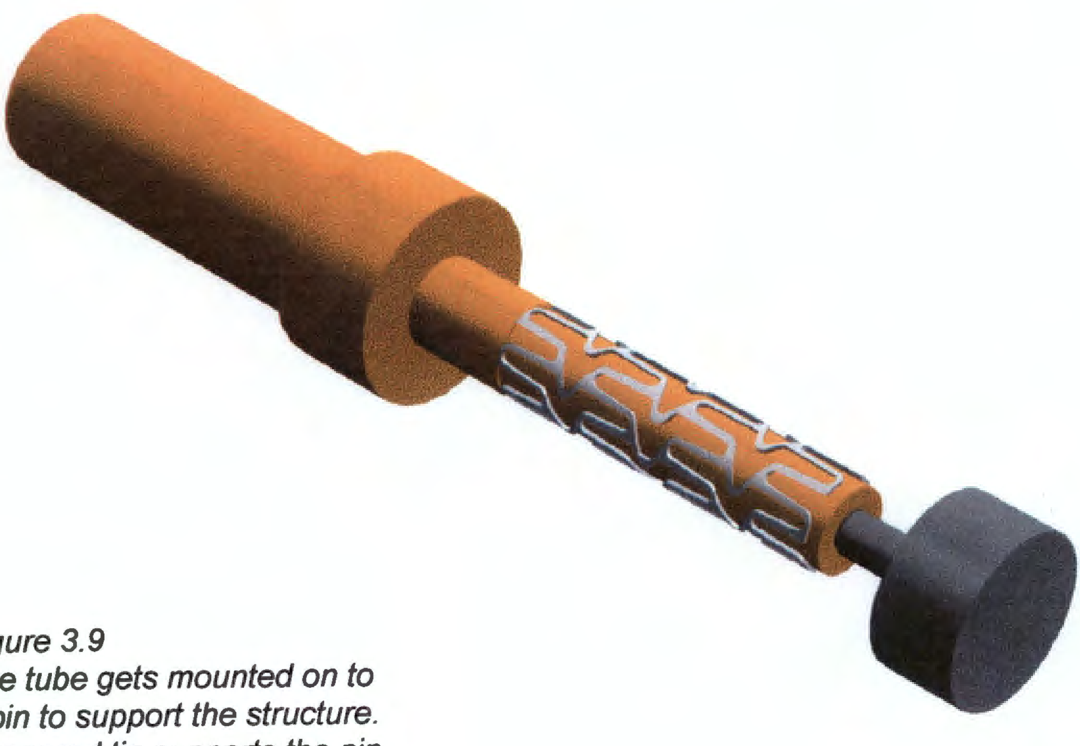


Figure 3.9
The tube gets mounted on to a pin to support the structure. A tapered tip supports the pin at its distal end.

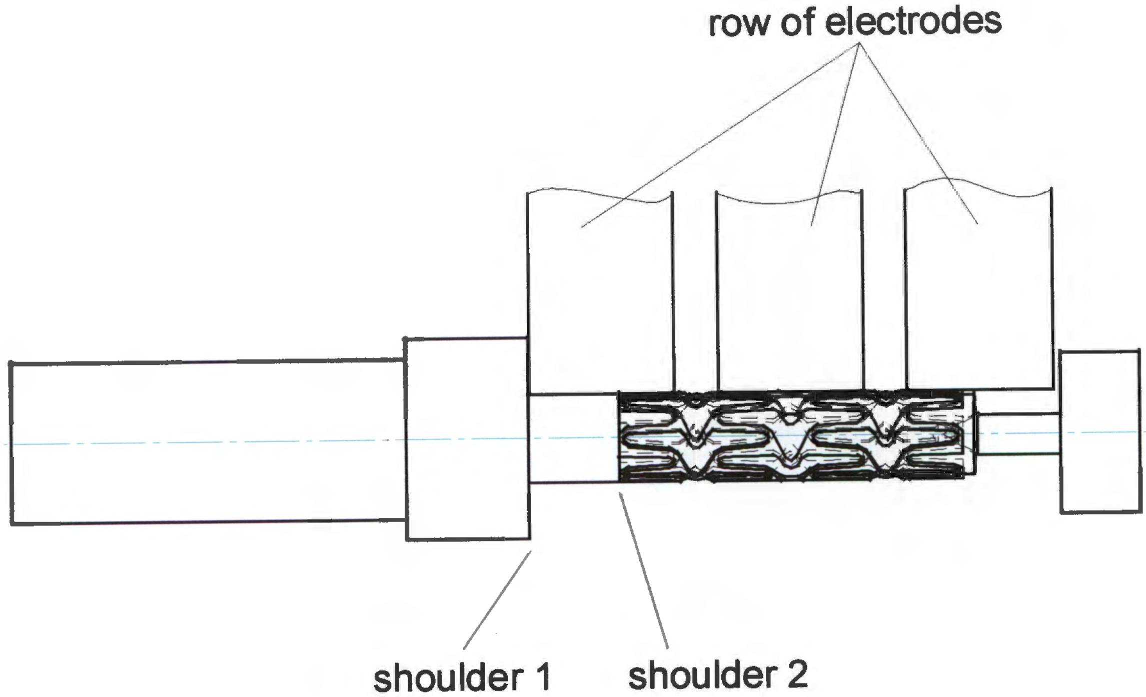


Figure 3.10 *The tube gets pushed against shoulder 1. When the electrodes just touch shoulder 2 they are correctly positioned relative to the tube.*

CHAPTER FOUR

PROTOTYPING

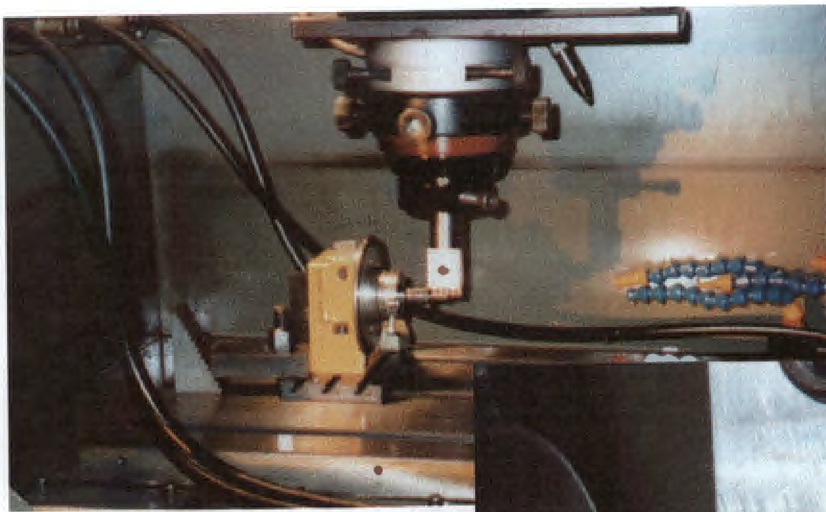
4.1 Manufacture of Initial Prototypes

Following the design process, prototypes of stents were manufactured. All prototypes were manufactured using the spark erosion technique. The electrodes were wire cut from solid copper plates. All other tools and appliances were manufactured using common mechanical workshop equipment, like a lathe and milling machine. For prototyping the spark erosion machine was equipped with a standard manual indexing head, that, besides other angle steps, allowed the rotation and positioning of the tubes every 30^0. The first samples of design 1 were sparked using standard machine settings. The samples were analysed, problems identified and the parameters changed accordingly to gradually improve the overall outcome of the spark erosion process. The evaluation of machining parameters and spark gaps was used as a basis for design 2.

Procedure

For the first prototypes a tube was machined out of a solid 316L rod, leaving a solid piece of material on one end to hold the workpiece in the clamping ring of the indexing head. The indexing head with the tube were aligned and centred to the electrode holder (Figure 4.1). This process is described in detail with the manual for the manufacture of a coronary stent in Appendix C.

These first prototypes were primarily used to adjust the machine parameters. Several settings can be changed that influence the outcome and speed of machining. The 4 most important parameters are: current I, gap voltage U, pulse length t and the spark time/ flush time ratio. Each of them can be set according to the workpiece and tool electrode size and the materials used. The precision of machining and the surface finish are determined by the size of the sparking craters found on the cutting edges. Their size is influenced by the material properties and by the discharge energy E (Equation 4.1)



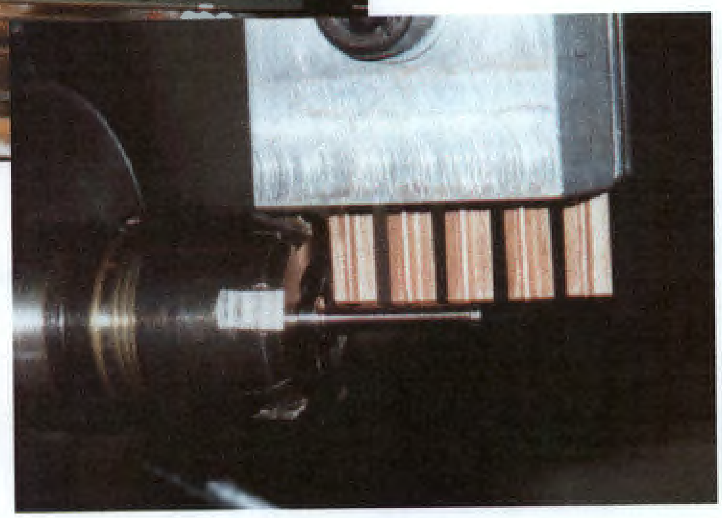


Figure 4.1
The set of electrodes gets positioned centrally to the tube and aligned with the tube's longitudinal axis.

$$E = U * I * t \qquad (4.1)$$

Each of the factors current I, gap voltage U and pulse length t similarly influence the discharge energy E. A machining process with all three of these parameters set to their lowest value will deliver small sparking craters and with this the best surface finish. It will, however, decrease the stock removal rate and so increase the total machining time.

For the stent, a good surface finish and precise machining are more important than the machining time and for that reason the machine was adjusted to low energy parameters. In order to avoid debris catching in the spark gap and causing interference, the sparking process has sparking and flushing cycles. During the flushing cycle the electrodes are lifted off the workpiece and the debris is flushed away with a current of dielectric fluid. Typically the values for spark time and flush time are in the magnitude of 1 to 2 seconds.

The values of the parameters in the final process are listed in the manual for the manufacture of a coronary stent in Appendix C.

After setting the machining parameters the work area of the spark erosion machine was closed and flooded with dielectric fluid, the sparking cycle was started (Figure 4.2).

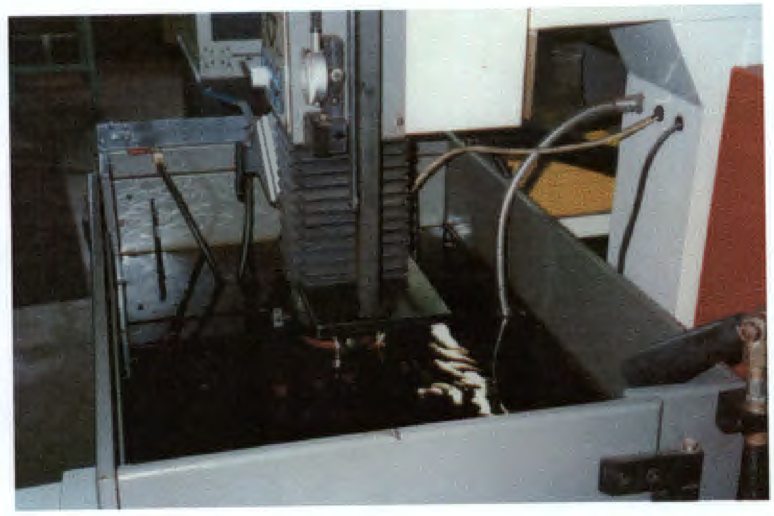


Figure 4.2
The spark erosion process within dielectric fluid.

The first row of openings was machined until the electrodes broke through the tube wall completely. The electrodes were then withdrawn, the indexing head was shifted by 60^0 and the next row of openings was sparked. Repetition of this process results in 6 rows of openings around the circumference.

The machine table was then shifted in the direction of the longitudinal axis of the tube and the indexing head by 30^0 to spark the second set of openings similarly to the first one.

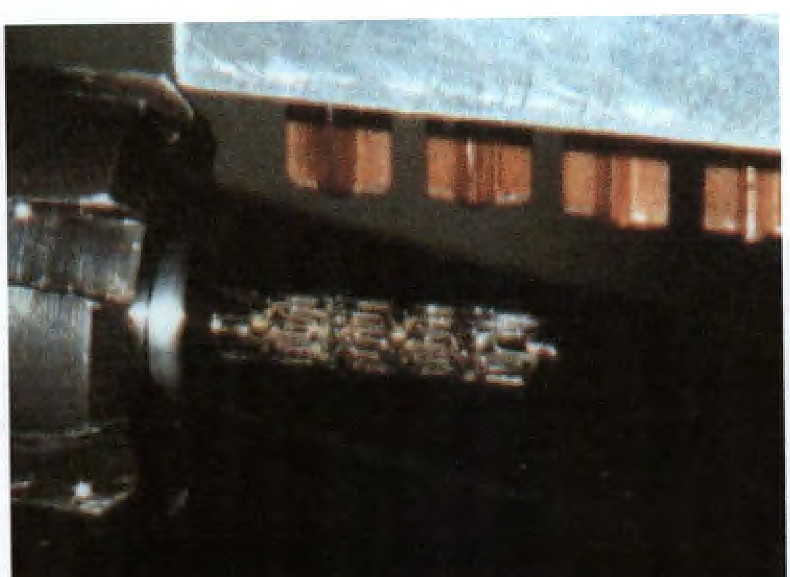


Figure 4.3
6 rows of openings around the circumference after repeated machining of rows of openings in 60^0 steps.

For each of the sparked rows, the machining parameters were slightly changed to see their influence on the outcome of the erosion process. To improve the overall stability of the slotted tube during cutting and to decrease burrs on the edges of the inner tube surface, an aluminium core was inserted into the tube in the later samples. For the last sample of the design 1 variety a tube cut to its final length was mounted on to a tube holder pin (see 3.2.4, Figure 3.10).

The samples were inspected optically under a microscope and their dimensions were measured with a shadowgraph (Figure 4.4).

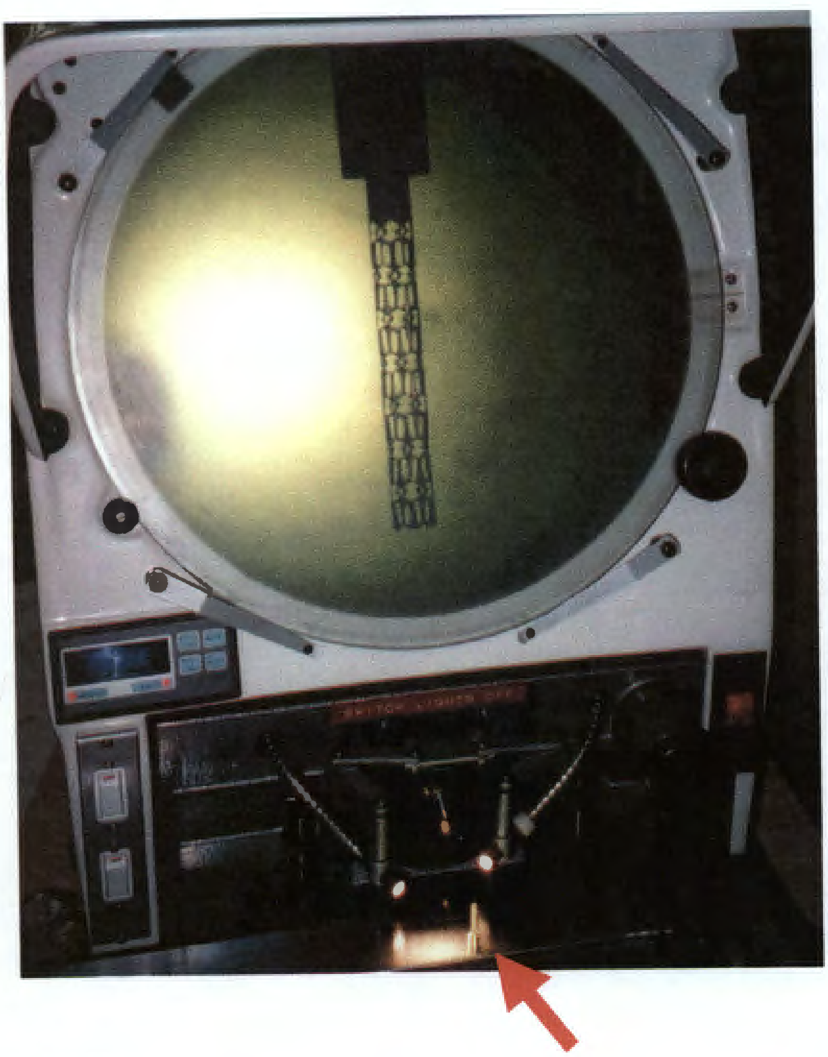


Figure 4.4
A shadowgraph image of an initial design sample. A 'to scale' image of the stent (arrow) is projected onto the screen. A scaling device allows measurement of the dimensions.

Results

The method of spark erosion delivered roughly the desired geometry of the initial prototype (Figure 4.5). A constant improvement to the quality of the manufactured samples could be achieved by adjusting machining parameters and conditions.

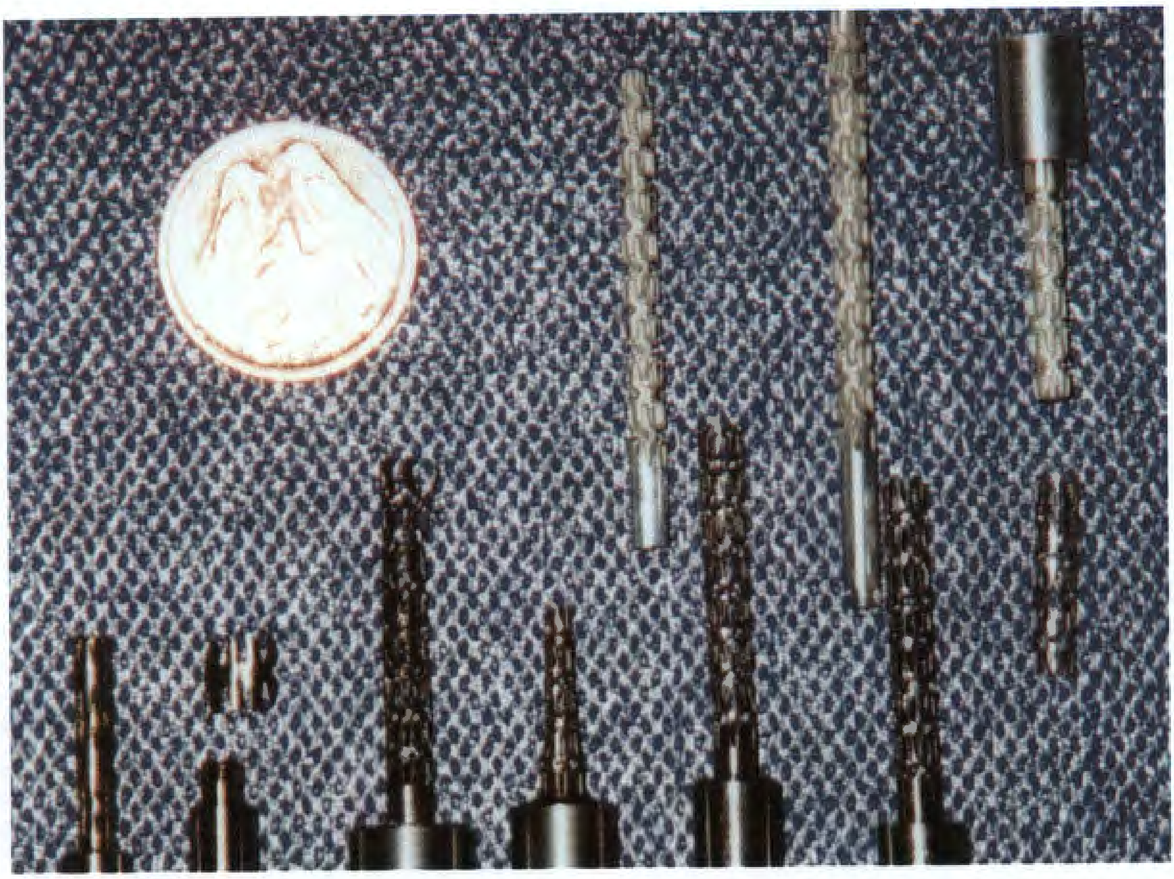


Figure 4.5 *Early samples of the initial design. The initial choice of machining parameters resulted in broken through struts (first and second from left). In subsequently sparked samples, struts broke in the region of the free end of the tube (third from left) The introduction of an aluminium core improved the quality of the samples (second and third from right). Finally a tube got mounted on to a pin serving as core and tube holder (right). A South African one cent coin that is 15mm in diameter is shown for size comparison (top left).*

The first two samples broke at their strut connections because the discharge energy was too high, causing large spark gaps between the electrode and workpiece which resulted in narrow, fragile struts. Adjusting the of machining parameters to lower discharge energy levels (on-time vs off-time ratio decrease) resulted in an increased strut width and the complete pattern of openings could be sparked into the tube. Still, the precision at the free end of the structure was insufficient and some struts in this area broke. This was found to be due to deformation of the, with the progress in cutting of openings, increasingly weakened tube structure. The misalignment of the tube relative to the electrodes was highest at the free end. Improvement was achieved by introducing a tight fitting aluminium core into the tube. This supports the tube and prevents deformation of the tube during the manufacturing process. It was also found that the core has a positive effect on the formation of burrs at the edges of the inner surface of the tube. Eventually a tube cut to the final length was sparked while mounted on a tight fitting pin.

4.2 Manufacture of Final Prototypes

The redesigned samples of the final prototypes were manufactured using the machine settings evaluated while cutting the initial design. The openings were cut into a tube of 1.8mm diameter.

Procedure

The manufacturing procedure for design 2 prototypes corresponds to the procedure described for the manufacture of the last design 1 samples. Pieces of 316L tubing were machined to final length and fitted tightly onto the support pin as described in detail in the 'Manual for the Manufacturing of a Coronary stent' in Appendix C.

Results

The first samples of the final design showed geometric irregularities that were more significant than in the initial prototypes because of the smaller overall dimensions of the design. To eliminate these irregularities and to finally achieve a suitably refined manufacturing method, problems were identified and analysed and appropriate measures taken to improve the manufacturing.

Prototypes showed geometric irregularities in the region of the links (Figure 4.6). The width of all the links throughout the stent was not constant. Non-symmetry of the geometry of the electrodes leads to decreased strut widths on one side and increased strut widths on the other side of the links (Figure 4.6). An uncompensated backlash in the wire-cutting machine that was used to manufacture the electrodes resulted in a shift of centre points of the two relevant radii of 0.03mm (Figure 4.6). A set of new electrodes was wire cut, this time with programmed backlash compensation. Symmetrical electrodes with tolerances of less than +/-0.01mm were wire cut as a result.

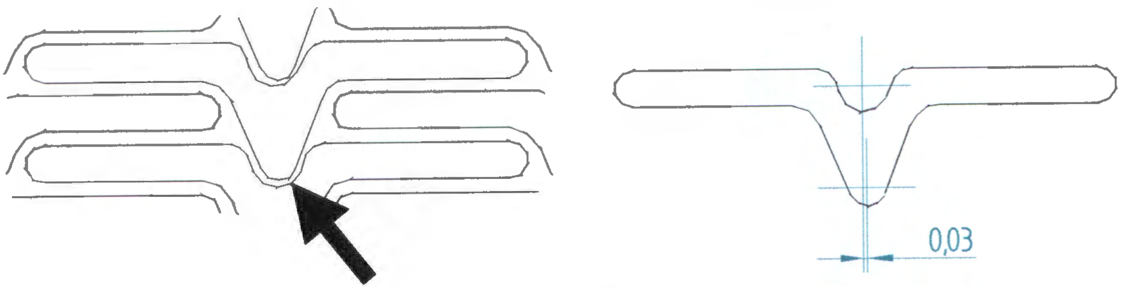


Figure 4.6 Irregular width of the links (left) caused by non-symmetrically cut electrodes (right).

Later on prototypes showed geometric irregularities particularly in the region of the free end of the support pin. These irregularities were worse around the rows of openings that are cut towards end of the cutting process. Residual internal stresses in the tube material or the tube holder pin material seem to cause deformation of the tube/ pin assembly when material stock is removed from one region, leaving an imbalance of internal stresses in the material. Local heating of the materials caused by the spark erosion process may contribute to the internal stresses and deformation. The tube and pin assembly deforms slightly after every row of openings that are cut. Cutting of lines of rows next to one another removes even more material stock from one region and increases the non-symmetric stress distribution (Figure 4.7). To restrict movement of the tube/ pin assembly caused by deformation, a tip that allows only rotation of the pin (Figure 3.11) supports the free end. To reduce the tendency of unevenly distributed stresses causing deformation, the sequence of cutting the openings around the circumference was changed in a way that the cross section would always be as symmetrical as possible (Figure 4.7)('Manual for the Manufacturing of a Coronary Stent' in Appendix C). This kept longitudinal deformations to a minimum.

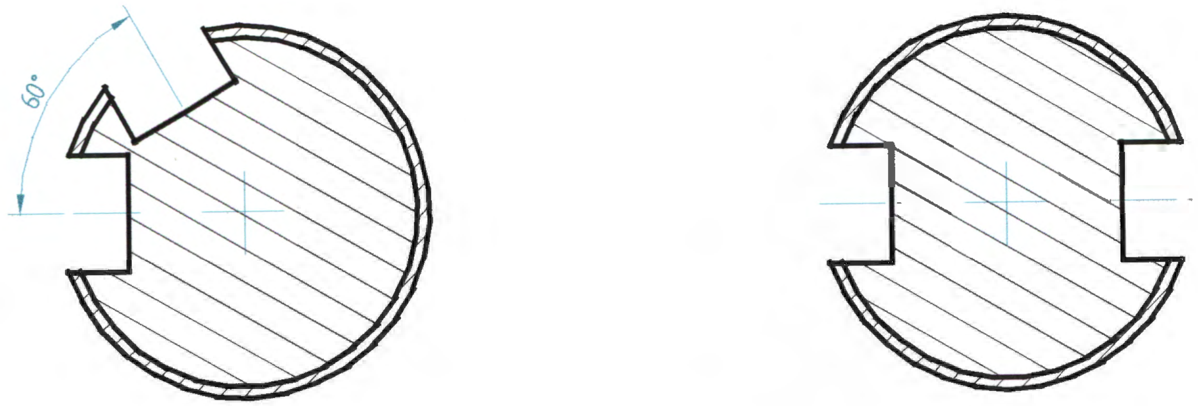


Figure 4.7 *Cross section through the tube/ pin assembly. Stock removal mainly from one side leaves a non-symmetrical cross section (left) with an unfavourable distribution of stresses leading to longitudinal deformation. Change of the cutting sequence aims to keep the cross section as symmetrical as possible throughout the manufacturing process.*

Several stents based on the final design were manufactured using the described manufacturing technique (Figure 4.8).

For comparison, the final design was also laser cut by an experienced European laser cutting company (Figure 4.9). The design was changed slightly in the region of the linkeages, as laser cutting allows for a more defined geometry.

Although this prototype is still very rough compared to how the stent should look, it proves the general feasibility of the manufacturing method but also shows its limitations. This is particularly obvious after examining the laser cut specimen (Figure 4.9). The limitations of the spark erosion technique in terms of the precision and surface roughness can most probably be overcome by further refinement of the sparking technique. Nevertheless it turns out that an improvement of end finish can only be achieved by further increasing the manufacturing time, which exceeds at present 2.5 hours per stent. This does not seem to be feasible, knowing that more sophisticated technologies are available.

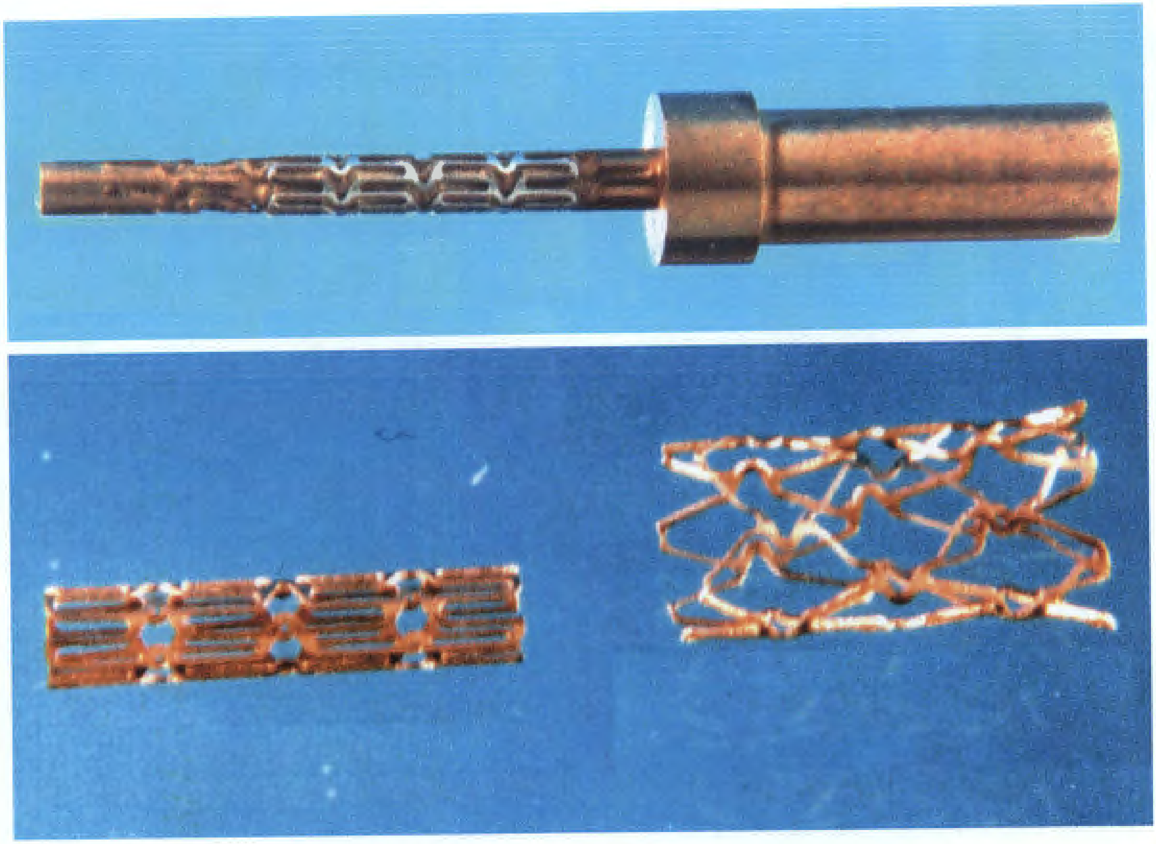


Figure 4.8 *Spark eroded tube of the final design on its support pin (top) and bare (bottom) in the manufactured and deployed state.*

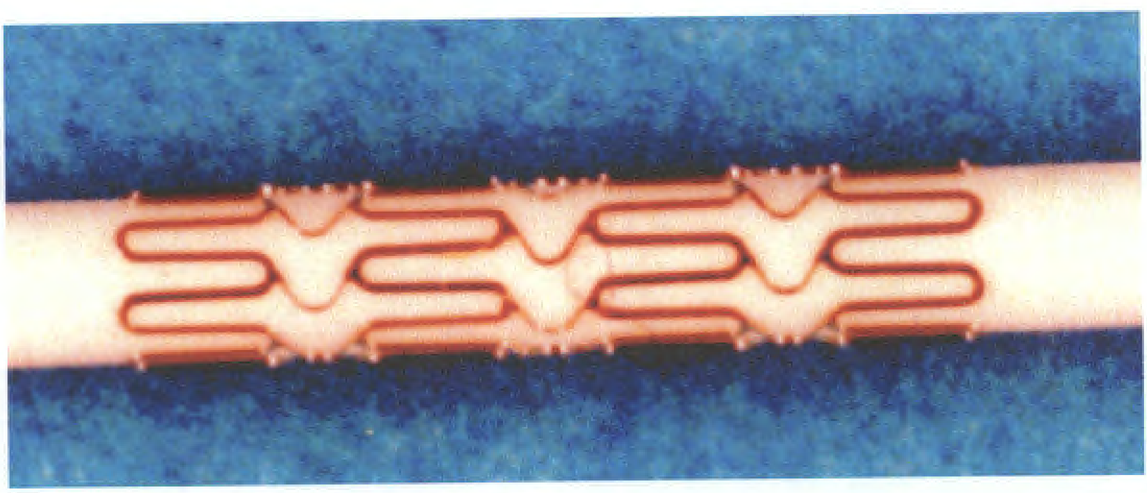


Figure 4.9 *Laser cut final prototype.*

CHAPTER FIVE

TESTING

5.1 Design and Prototype Testing

The European Community sets out the requirements for vascular implants and stents in particular (European Committee for Standardisation, 1997and 1998). For approval of such implants on the European market, a number of standard testing procedures for coronary stents need to be performed. Although there is no such legislation in South Africa yet, some of the recommended mechanical tests were performed to evaluate the performance of the stent design used for this project.

The material used is the medical grade stainless steel, that is used for most other self expanding slotted tube stents, and has shown to have only a moderate thrombogenicity during years of successful application (Palmaz, *et al.,* 1998). Therefore haemocompatibility, cytotoxicity and electrochemical tests were not performed.

Neither the geometry nor the strut and wall-thickness of the current design differ significantly from those of existing balloon expandable corrugated ring designs, for example the *JoStent* or the *NIR Stent (Figure 3.4).* For this reason it was anticipated that the design meets the requirements for stent radial compliance and deployment. However, the mechanical properties of the current design were tested in a computer simulation as well as in physical tests. The finite element analysis (FEM) shows the theoretical deformation of the stent structure during deployment and areas of critical stresses. It was followed by simple mechanical experiments, namely testing the expansion behaviour of the implant by deploying it with a PTCA balloon catheter and radial strength tests.

The surface of the final prototypes was left unpolished based on the non-satisfactory surface quality as a result of the spark erosion process. For this reason surface tests were not undertaken, however electron microscopic inspection of several prototypes was performed to point out problems with the manufacturing method.

5.2 Finite Element Analysis

The design of the stent prototype was analysed using the ABAQUS™ (Hibitt, Karlsson & Sorensen, Inc. 1997) software package. A three-dimensional computational model of the stent structure was created and used to simulate its mechanical deformation behaviour.

5.2.1 Materials and Methods

Inflating a cylindrically shaped balloon inside the tubular stent lumen results in deployment of the implant. Hereby the openings encompassing the circumference of the stent are stretched, allowing for a larger circumference and diameter.

In a very simple model the complex structure of the perforated stent wall can be broken down to a series of individual members forming a lever and hinge system (Figure 5.1).

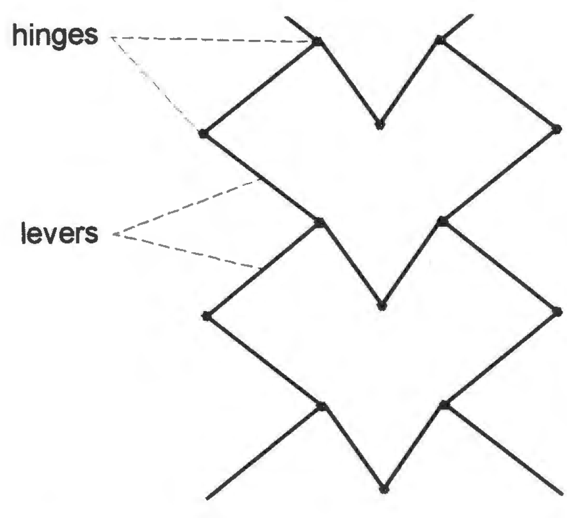


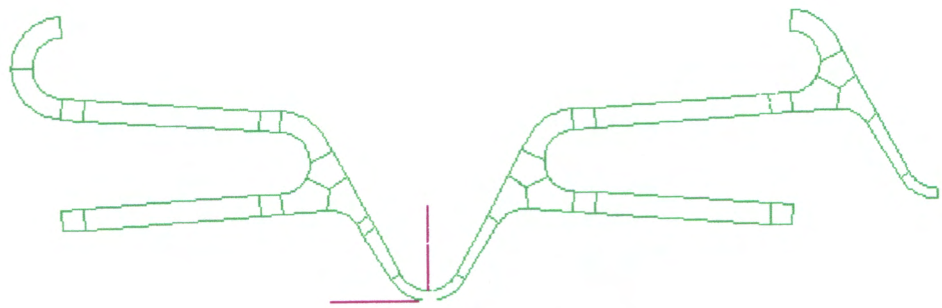
Figure 5.1 Simplified structure of the stent wall.

The system of levers and nodes from Figure 5.1 can be described mechanically by assigning an equation to each individual lever and assembling the levers in a way that equilibrium of forces and compatibility of displacements are satisfied at each hinge point. The assembled structure is described by a system of the equations of its members.

Matrix based, computer aided numerical solution of a system of equations forms the basis for finite element analysis of mechanical deformation of the structure. Unlike in the very simplified example of Figure 5.1, the real continuum structure of the stent wall does not consist of simple linear elements with natural subdivisions at hinge points. It has to be subdivided into a finite number of elements interconnected at a number of node points of their common boundaries (Figure 5.4). For two-dimensional and shell models, these elements are usually chosen to be rectangular or triangular in shape depending on the complexity of the geometry. The nature of finite element analysis is that the accuracy of the solution increases with the number of elements into which the structure has been divided. This, however, increases the complexity of the problem and the computer time required. For this reason, the number of elements used should be kept to a reasonable quantity (Rockey *et al.,* 1975).

The geometry of the stent implant was modelled as a shell structure, a simplification based on the assumption that the deformation of the structure while changing the diameter of the tubular geometry mainly takes place in a cylindrical plane encompassing the circumference of the stent. Deformations normal to the plane as well as changes of the wall thickness were expected to be minimal and could therefore be neglected. The surface model is the infinitely thin middle layer of the tube wall flattened out in a plane.

The openings in the stent surface are defined by the cutting edges of the spark erosion process (Figure 3.6). The geometry of the computational model was created in a similar way by intersecting the – in this case flattened out - surface of the implant with the electrode surfaces, creating an array of cutting edges forming a wire model. Filling surface elements into the wire model created the model surface (Figure 5.2). Size and shape of the surface elements were chosen in a way that supported their convenient subsequent breaking up into finite elements. To define the number of elements per surface, mesh seeds were put into place at the edges of the contacting surfaces. Mesh seeds are preferable points for the situation of nodes. In regions with large expected deformation, like the radii, the mesh was chosen to be denser to increase accuracy of the analysis. Regions with expected small deformation, like the straight levers, only need few elements and more widely distributed seeds (Figure 5.3).



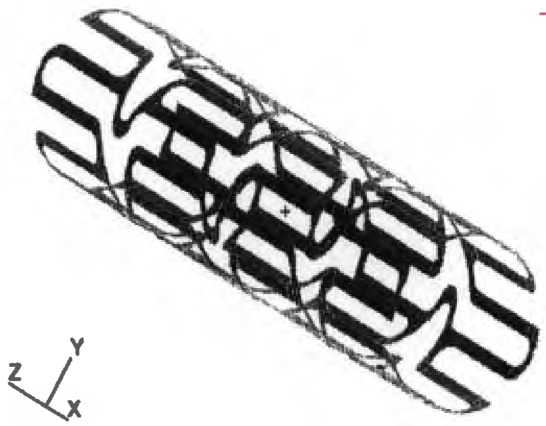


Figure 5.2
Wrapped surface model of the middle layer of the stent wall (left) composed by several surface elements (top).

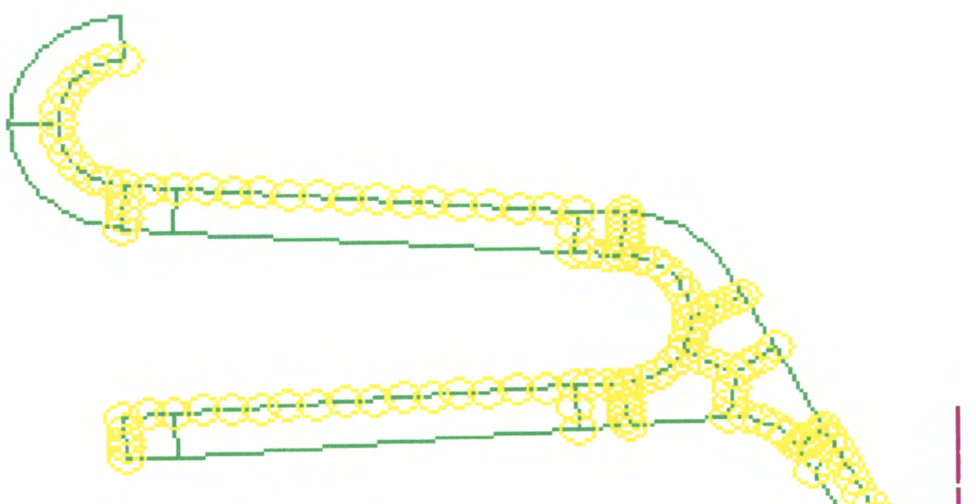


Figure 5.3
Seed nodes (yellow) define the number of finite elements per surface. Many nodes in areas of expected large deformation result in a dense mesh of finite elements there.

Outcome of the meshing was a shell model of the stent composed of 4644 shell elements that are linked by 5850 nodes (Figure 5.4).

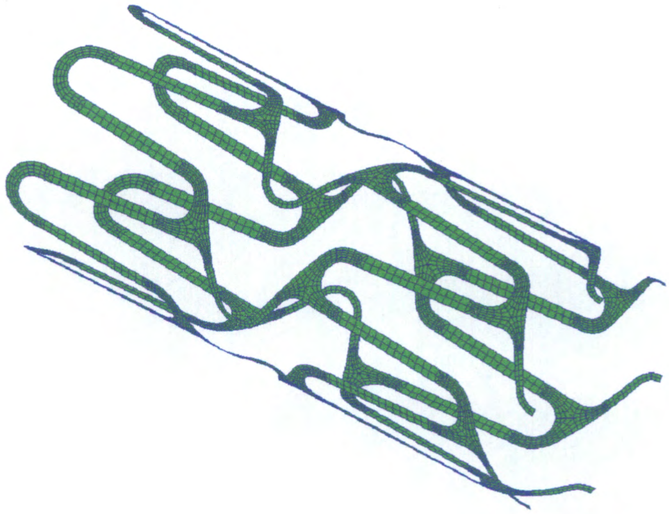


Figure 5.4 *Model of the middle layer of the stent wall composed of finite elements. The surface is already wrapped to a tube. Only half the stent is shown, as it is symmetrical about its mid-line.*

5.2.2 Analysis and Results

The finite element model was used to simulate the mechanical deformation process of the stent as a consequence of balloon deployment. A elastic-plastic analysis using a von Mises plasticity model[5.1] was performed. The input deck in Appendix D describes the steps undertaken and shows the data entered for the analysis. The finite element analysis was run by applying a pressure of 5 bar onto the inner surface of the stent model, causing its deployment within the lumen of a modelled, rigid tubular vessel of 3.5mm diameter. The stent was fully deployed when it touched the vessel wall.

The simulated deformation of the openings was equivalent to a stent deployment of 3.5mm (Figure 5.7) and showed a regular geometry without kinks or areas of excessive deformation. The applied pressure of 5bar was sufficient to open the stent completely. Deformation and resulting peak stresses were higher in the radii of the stent structure than in the straight levers. The peak plastic strain was found to be 11% (Figure 5.5) and the von Mises equivalent stresses did not exceed 345MPa (Figure 5.6).

[5.1] Von Mises equivalent stresses represent the six different stresses occurring in plastically deformed models. Van Mises plasticity models are used to describe the plastic deformation stresses in three dimensional isotropic models.

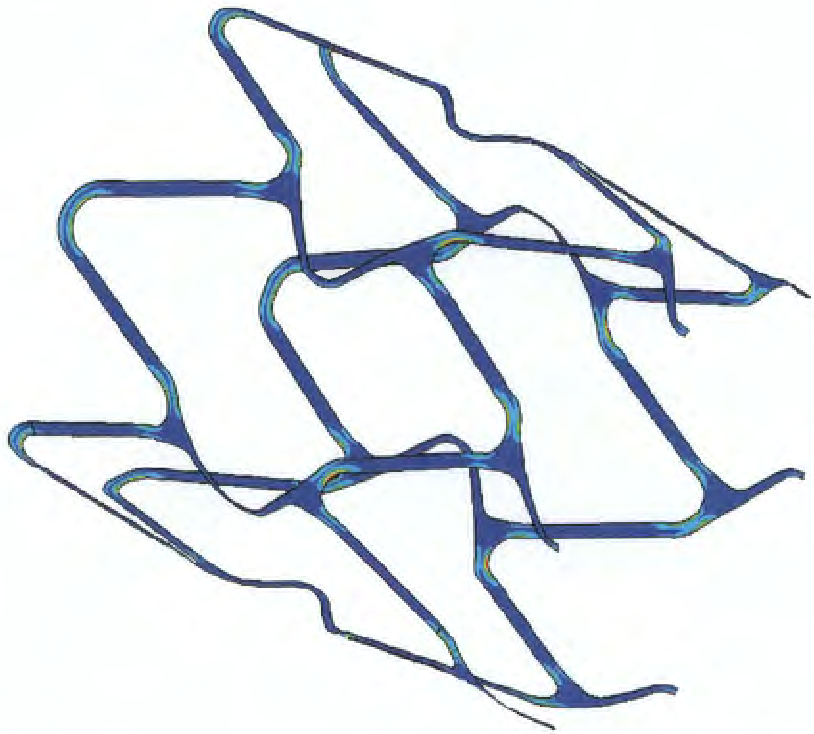


Figure 5.5 *Finite element model of the stent deployed to 3.5mm showing areas of permanent (plastic) deformation in the stent. The peak plastic strain is in the region of 11%. The ultimate strength of the material is reached at approximately 40% strain.*

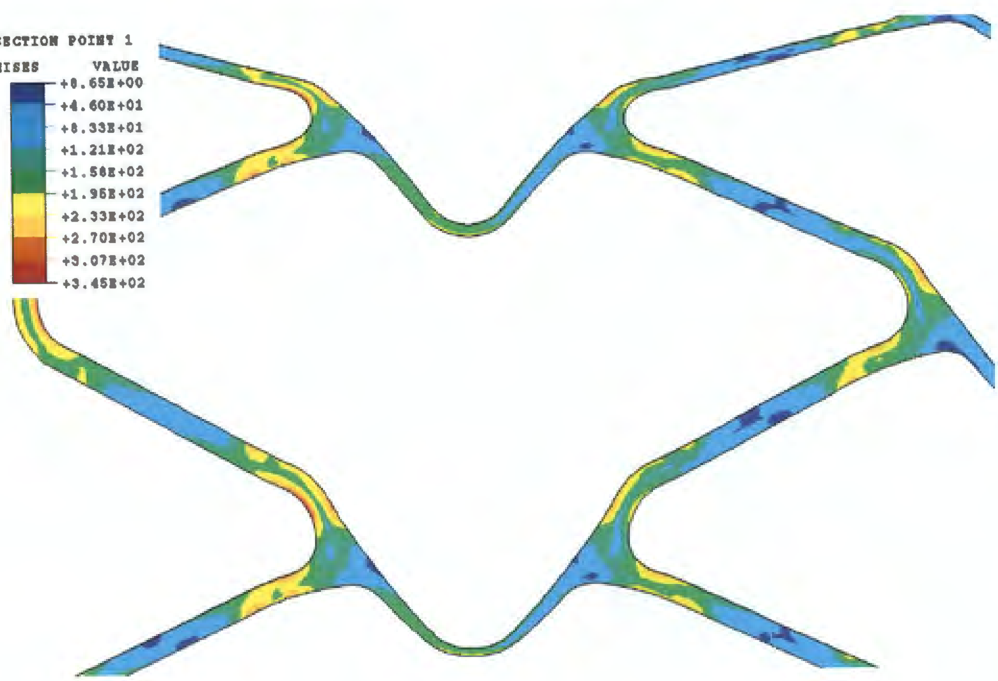


Figure 5.6 *Detail of a stent opening showing the von Mises equivalent stresses in the wall of the structure represented by different colours. The peak stress is 345MPa, which is 75% of the ultimate strength of the material.*

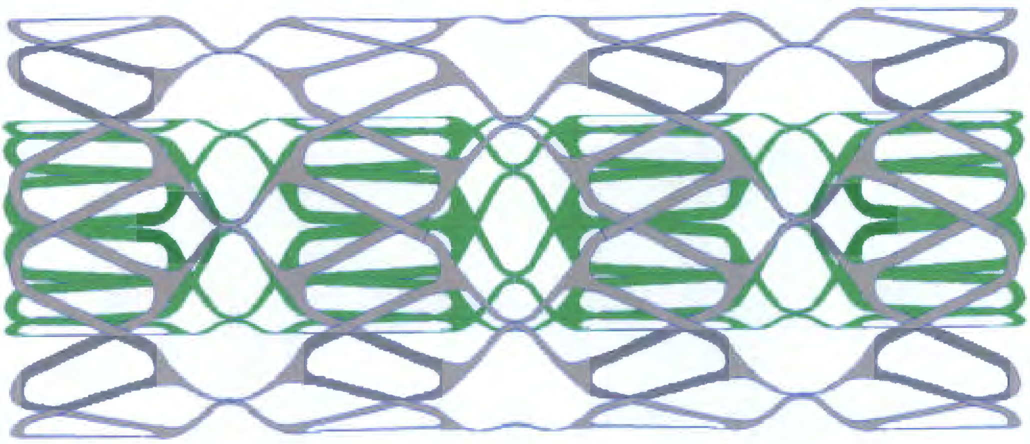


Figure 5.7 Complete model of the stent showing the geometrical change when deployed to 3.5mm.

5.2.3 Discussion and Conclusion

The finite element analysis simulated the stent's primary mechanical action, its deployment inside a tubular structure. The applied internal pressure expanded the modelled structure radially against a rigid, tubular constraining surface, simulating a vessel.

The uniform deployment of the stent cells without kinks or excessively deformed areas points to an appropriate geometry for the application of a radially expandable tubular structure within the given limits. It could also be shown that the inflation pressure of 5bar would be sufficient to deploy the stent fully. Analysis using lower pressures have not been performed since typical inflation pressures of PTCA balloons for stent placement vary from 8bar up to above 20bar and a secure deployment with standard PTCA balloons is guaranteed. It can be concluded that the designed stent deploys uniformly at an appropriate pressure.

The maximum plastic deformation and peak von Mises stresses were reached in the areas of the radii in the corrugated rings. The struts connecting the radii only underwent minor deformation, functioning as 'levers' in between 'hinge' areas, similar to the 'lever hinge model' from Figure 5.1. The moderate plastic strains in deformation areas reaching only 11% leave a comfortable 2/3 gap to the ultimate strain of 40% above which the material would fail. The von Mises equivalent stresses in this model of 345MPa also only reach about 75% of the given 490MPa strain at failure. The analysis shows that during normal functioning the deformations are well within the non-critical range

The numerical modelling is based on the designed geometry with the absence of any manufacturing variations. Since manufacturing involves tolerances, the gathered results must also be used to address the failure mechanism of the stent. The stent struts will fail if the local deformation exceeds a critical value. It is important to know whether any areas of the device are very sensitive to minor changes in. In such areas, either the design can be changed or the allowable tolerance can be kept sufficiently small to ensure the correct sizing of struts. This aspect has however not been analysed.

5.3 Mechanical Testing of Stent Deployment

The stent gets deformed from its manufactured diameter to its lowest diameter when crimped onto the deflated PTCA balloon. At implantation the stent gets deployed to its implanted diameter as a result of balloon inflation to its nominal pressure. The change of stent diameter during crimping and deployment causes plastic deformation of the stent structure as it was simulated in the previous section (Section 5.2). An easy test of mechanical stent action therefore is to test the crimping of the stent onto the inflatable balloon part of a PTCA catheter and its deployment. The practical test of mechanical stent action can be used to verify some results of the computer simulation.

5.3.1 Materials and Methods

A specimen of the final spark eroded prototypes was crimped onto a deflated PTCA balloon of 3.0mm nominal diameter (Figure 5.8). The balloon was placed under a light microscope with an attached video imaging system and was slowly inflated while a video film was recorded (Figure 5.9). The inflation pressures needed to start stent deployment and the pressure needed to fully deploy a stent to an overall cylindrical shape were also recorded.

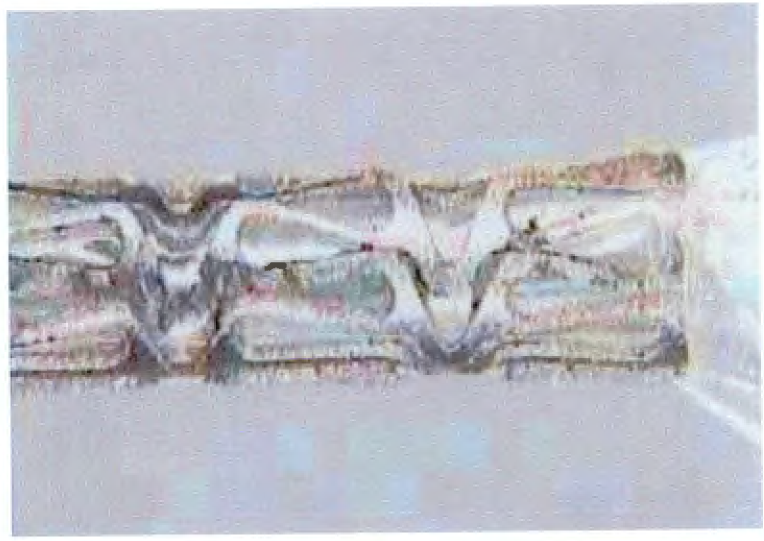
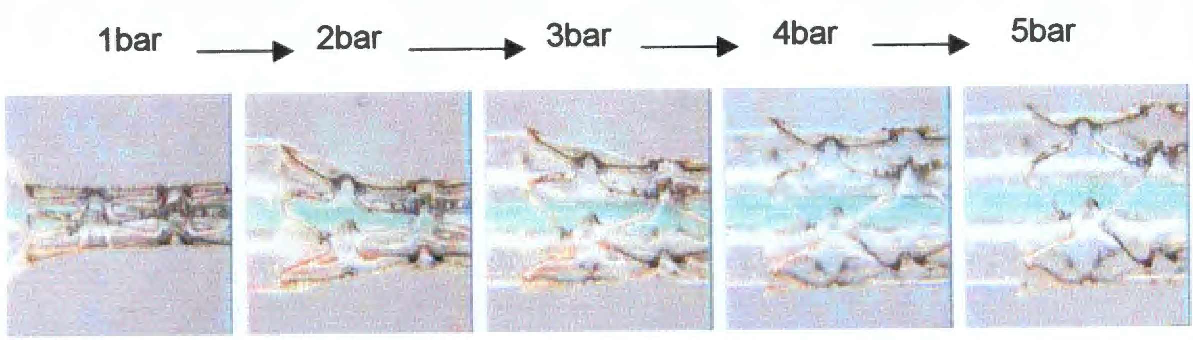


Figure 5.8
Specimen of the final prototype crimped onto a PTCA balloon.

5.3.2 Results

The stent could be crimped onto the balloon tightly. Inflation of the balloon lead to deployment of the stent starting from both its ends towards the centre, causing initial end flaring. Deployment started at about 3 bar and a full cylindrical shape of the stent was reached at 5 bar.



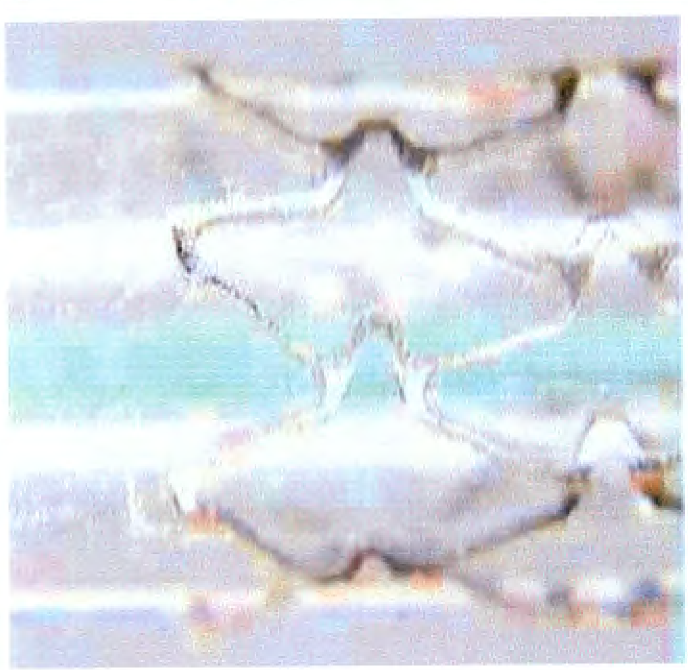


Figure 5.9
Inflation of the PTCA balloon and deployment of the stent (top from let to right). The fully deployed stent and balloon (bottom).

5.3.3 Discussion and Conclusion

The stent reached its fully deployed diameter at below 5 bar balloon inflation pressure. This confirmed the results of the simulated finite element analysis deployment, where a final pressure of 5bar was used. As discussed in section 5.2.3 this lies well within the typical inflation pressures of current PTCA balloons, showing that the stent can be fully deployed. One must note that the diameter only increases insignificantly beyond the pressure (e.g. 6bar), at which the nominal balloon diameter is reached (some 0.1mm). Testing at higher pressures, like they would be used to crack hard plaques inside the artery, barely influences the final diameter and was therefore not included.

The mechanism of expansion of the stent wall openings (Figure 5.9) could be seen to be similar to that anticipated from the results of the computer simulated deployment (Figure 5.5). As in the computer model there were no areas of excessive deformation and the corrugated ring structure expanded similar to the 'lever and hinge' system shown in Figure 5.1. The fact that the deployment was acceptable despite the relatively poor tolerances achieved in the prototypes shows that the design is relatively robust in terms of dimension deviation in strut width and the outcome of mechanical deformation at stent deployment. However, the occurring stresses and strains in the critical areas are not known and therefore the results cannot be used to define a safe range of manufacturing tolerances.

As opposed to the cylindrical deployment shown in the finite element model, the stent deploys from its ends towards the middle, showing initial end flaring ('hourglass' shaped deployment). Since the structure is homogenous throughout its length with no particularly stronger or weaker rings one expects cylindrical deployment. The reason for the flaring deployment was found in the typical way PTCA balloons are wrapped. This causes balloon deployment starting from the balloon ends, forcing the stent to deploy similarly.

5.4 Mechanical Testing of Radial Compliance

Another method of testing relevant mechanical properties of the prototypes is to measure their radial compliance. The tests of radial compliance for stents described in the literature are almost similarly performed by wrapping a non elastic, collar type of device around the stent. The free ends of the collar get tension loaded to compress the stent and the change of stent diameter or the dispalcement of the free collar ends are measured as a function of load (Agraval *et al.,* 1992; Fallone, *et al.,* 1988; Keane, *et al.,* 1995). The measured radial compliance of the stent prototypes was compared to radial compliance data of three other balloon expandable stents described by Keane, *et al.*, (1995).

5.4.1 Materials and Methods

A pressure-diameter ratio measurement setup with similar performance to the ones described by Fallone *et al.*, (1988) and subsequently used by Agraval *et al.*, (1992) and Keane *et al.*, (1995) was used. For camparison with data published by Keane *et al.*, paper collars and procedures similar to the ones described in their experiments were used. For this project there was access to a computerised Instron™ force displacement measurement appliance from which force displacement readouts can be taken directly (Figure 5.10).

Paper collars were cut out of the back cover of adhesive labels. They were found to have similar friction properties as the ones described in the literature by Fallone *et al.,* (1992) and Keane *et al.,* (1995) (Figure 5.10)

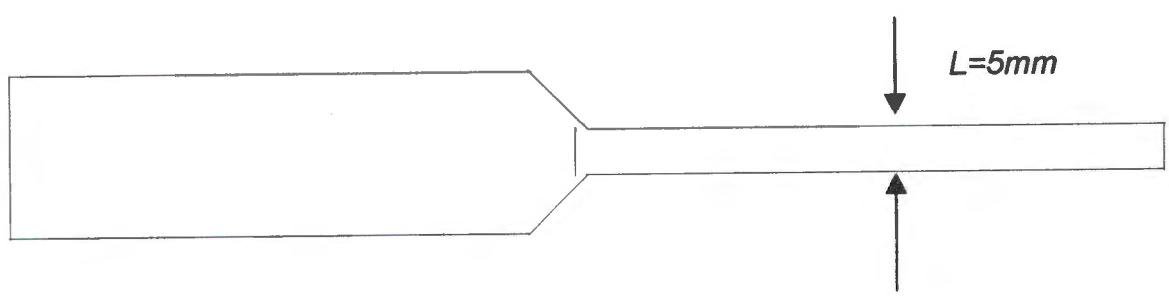


Figure 5.10 The paper collar was cut out of the backing paper used in adhesive labels.

The relation of measured linear displacement ΔK to resulting stent diameter D is defined by:

$$D = D_0 - \frac{\Delta K}{\pi}[mm] \qquad (5.1)$$

with D_o being the starting diameter. The stent tested had a starting diameter of D_o= 3.5mm.

In order to eliminate the influence of system elasticity caused by the wrapped paper collar, the force-displacement curve of the paper collar wrapped around a rigid 3.5mm core was measured. The data was used to normalise the results by subtracting the lengthening caused by system elasticity from the actual reading while testing the stent.

The paper collar was wrapped around the stent and the collar ends were clamped into the jaws of the Instron™ (Figure 5.11). The collar was loaded until it was almost tightly wrapped around the stent, then force-displacement readings were recorded. The equation developed by Keane et al., (Equation 5.2) was used to convert the applied linear force F into resulting global radial pressure P.

$$P = \frac{2F}{LD}[kPa] \qquad (5.2)$$

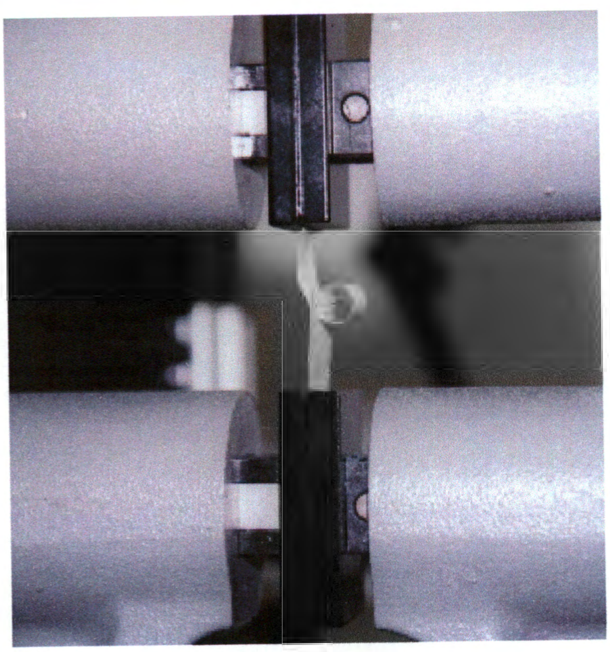


Figure 5.11
A paper collar wrapped around a stent (here still very loosely) with its ends in the jaws of a force-displacement measuring appliance.

To allow comparison with existing data, a relative diameter percentage D_r based on the ratio between starting diameter D_o and actual diameter D was used to describe diameter changes:

$$D_r = \frac{D}{D_0} * 100[\%] \qquad (5.3)$$

The readouts of the Instron™ are force displacement curves, characteristic for the stents. Two of the designed stents were tested. The data processed using equations 5.1 to 5.3 was compared to the radial strength data of the *Palmaz Schatz™*, the *Multilink™* , and the *AVE Micro™*[5.1] stent (Keane *et al.*, 1995).

5.4.2 Results

The force/ displacement data from the evaluation of system stiffness, the tests of both stent specimens (stent 1 and 2), their average force/ displacement data and the system stiffness compensated data of average force/ displacement is shown in Table 5.1 and Figure 5.12.

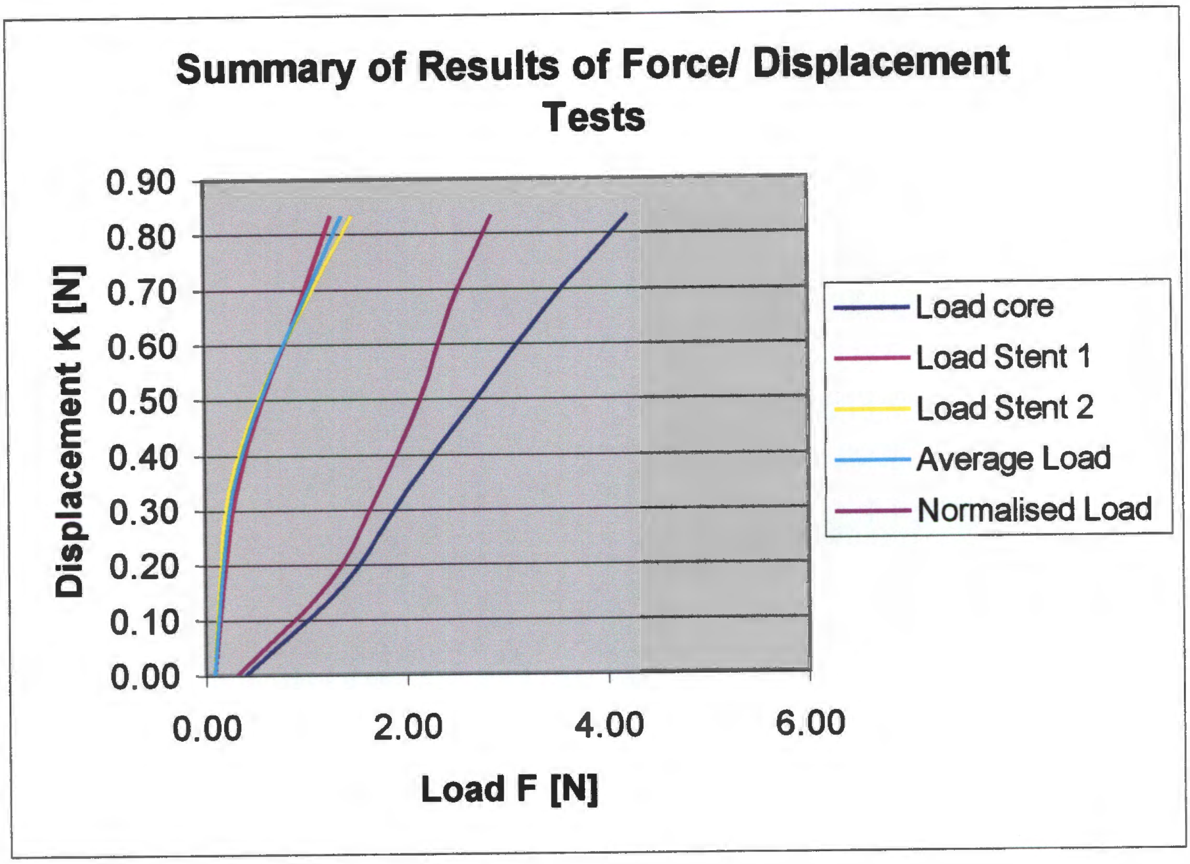


Figure 5.12 Results of three measurements: force/ displacement curves for two stent specimens (load stent 1 and 2, pink and yellow) and a rigid core (load core, blue). The displacement caused by the elasticity of the collar (system stiffness curve, blue) was subtracted from the displacement of the calculated average load/ displacement curve of the two specimens (average, turquoise). Result was an average load/ displacement curve of the two tested specimens (normalised load, purple), that is compensated for system stiffness.

[5.1] Applied Vascular Engineering, Inc. Santa Rosa, CA, USA

Displacement K [mm]	Load core F_c [N]	Load Stent 1 F_1 [N]	Load Stent 2 F_2 [N]	Average Load Stent 1 and 2 F_a [N]	Normalised Load F_n [N]
0.00	0.39	0.09	0.09	0.09	0.31
0.17	1.39	0.18	0.14	0.16	1.23
0.33	2.00	0.31	0.24	0.27	1.73
0.50	2.70	0.57	0.54	0.56	2.14
0.67	3.40	0.93	0.98	0.95	2.45
0.83	4.20	1.25	1.46	1.36	2.84
Estimated Deviation of Displacement: +/- 0.02mm	Estimated Deviation of Load: +/-0.07N Excluding Measurement at Displacement 0.83				

Table 5.1 *Data collected and calculated from force displacement tests of a rigid core and stent specimens.*

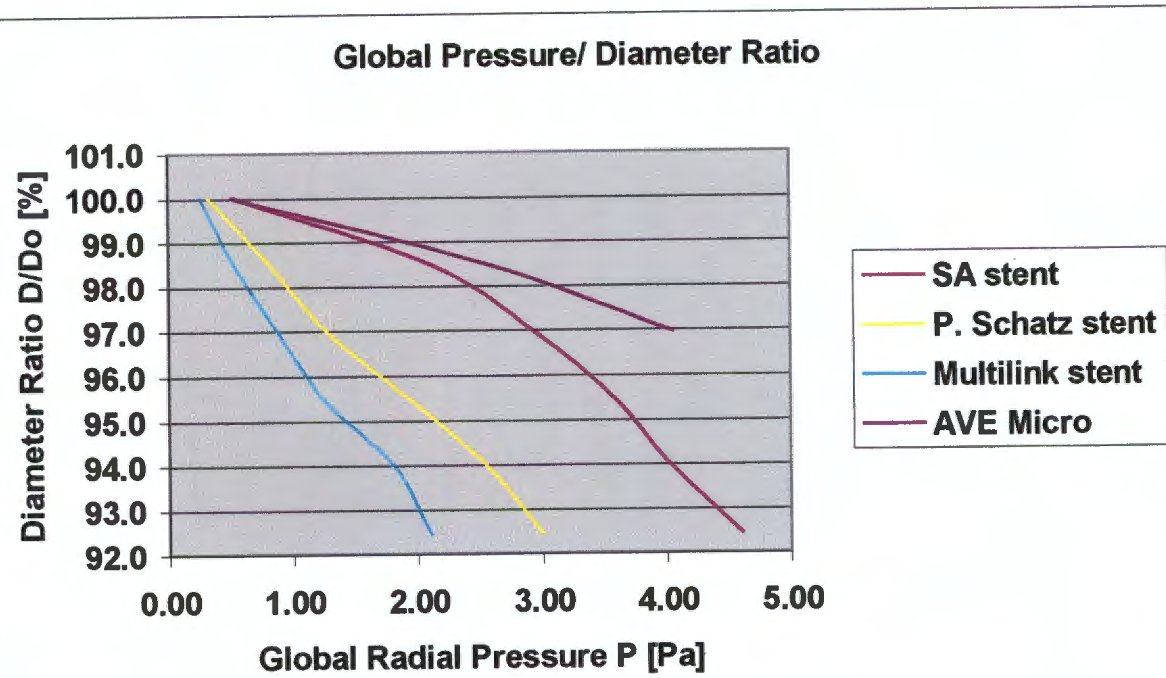


Figure 5.13 *The relative diameters of the designed stent (SA stent, pink), the* Palmaz Schatz™ *stent the* Multilink™ and the AVE Micro™ *stent are plotted against applied global radial pressure P. The radial strength of the designed stent exceeds the ones of the* Palmaz Schatz™ *and* Multilink™ *stents.*

The radial strength data for the *Palmaz Schatz™* stent and the *Multilink™* stent was extracted manually from the printed diagrams published by Keane *et al.*,

(1997) and the pressure unit converted from mmHg into Pa (Table 5.2). The Global radial pressure P versus diameter ratio D/D_0 were calculated (Equations 5.2 and 5.3) and extracted into a diagram (Figure 5.13)

Diameter D [mm]	Diameter Ratio D/D_0 [%]	Global Radial Pressure P [Pa]			
		SA stent	P. Schatz stent	Multilink stent	AVE Micro
3.50	100.0	0.54	0.33	0.26	0.51
3.45	98.5	2.11	0.82	0.54	2.57
3.39	97.0	2.94	1.28	0.88	4.04
3.34	95.5	3.58	1.95	1.25	-
3.29	94.0	4.02	2.55	1.80	-
3.24	92.5	4.60	3.00	2.10	-

Table 5.2 *Diameter ratio and pressure data collected and calculated for the designed stent, the* Palmaz Schatz™, *the* Multilink™ *and the* AVE Micro™ *stent.*

5.4.3 Discussion and Conclusion

The mechanical tests show that the radial strength of the designed stent exceeds the radial strength of the *Palmaz Schatz™* and the *Multilink™* stents but is below the radial strength of the *AVE Micro™* stent. There is no data of ideal radial strength for a coronary stent and none of the stents the designed stent was compared to therefore seems particularly suitable in terms of its radial strength. With the results of this mechanical test in conjunction with the results of the necessary inflation pressure from the finite element analysis (Section 5.2) and the deployment test (Section 5.3), it can be concluded that the designed stent meets all mechanical requirements for radial strength.

The used method for testing the radial strength of a stent delivered well reproducible results, manifested in the low deviation of data for both tested stents. The radial compliance data for the *Palmaz Schatz™*, the *Multilink™* and the *AVE Micro™* stent, however, were extracted from a printed diagram. Based on the naturally poor accuracy of such data gathering and based on the very qualitative nature of the result of the comparison an estimation of data deviation was neglected.

5.5 Scanning Electron Microscopy

To evaluate the quality of manufacturing by spark erosion and to compare it to the quality achieved using the laser cutting technique, scanning electron microscope (SEM) images of several prototypes were taken.

5.5.1 Preparation of Specimens and Microscopy

Three different specimens were glued to a specimen holder with conductive glue. This included one specimen of the final spark eroded prototypes, one specimen of the laser cut prototypes for comparison and one laser cut and electropolished specimen to demonstrate the outcome of electropolishing. The design of the laser cut specimen varies slightly from that of the spark eroded one, since laser cutting allows for a better defined geometry of the links.

The specimen holder tray was inserted into the microscopy chamber and the chamber was evacuated. After calibration of the electron beam, microscopy images of each of the three specimen were taken. These include overall (50x magnification) images as well as close up (400x magnification) images of the cutting edges.

5.5.2 Results

The overall image of the spark eroded specimen shows that the required geometry could be manufactured. None of the struts were broken or otherwise damaged (Figure 5.14). Irregularities of the geometry, like varying strut width throughout the structure were however obvious. Variations in strut width of up to 0.03mm were measured. The width of the link struts was found to be too large. Although the close up image of the spark eroded cutting edges discovers large craters and minor burrs, they are straight and regular (Figure 5.16).

The laser cut specimens of a design very similar to the final prototypes showed a regular overall geometry (Figure 5.15). Variations in strut width could not be measured. The close up image shows smooth, burr free cutting edges (Figure 5.17).

The polished specimen of the laser cut design variation shows, how state of the art electropolishing concludes the manufacturing process after cutting the stents out of a tube (Figure 5.18). A mirror-like surface and extremely smooth edges are the result of this process.

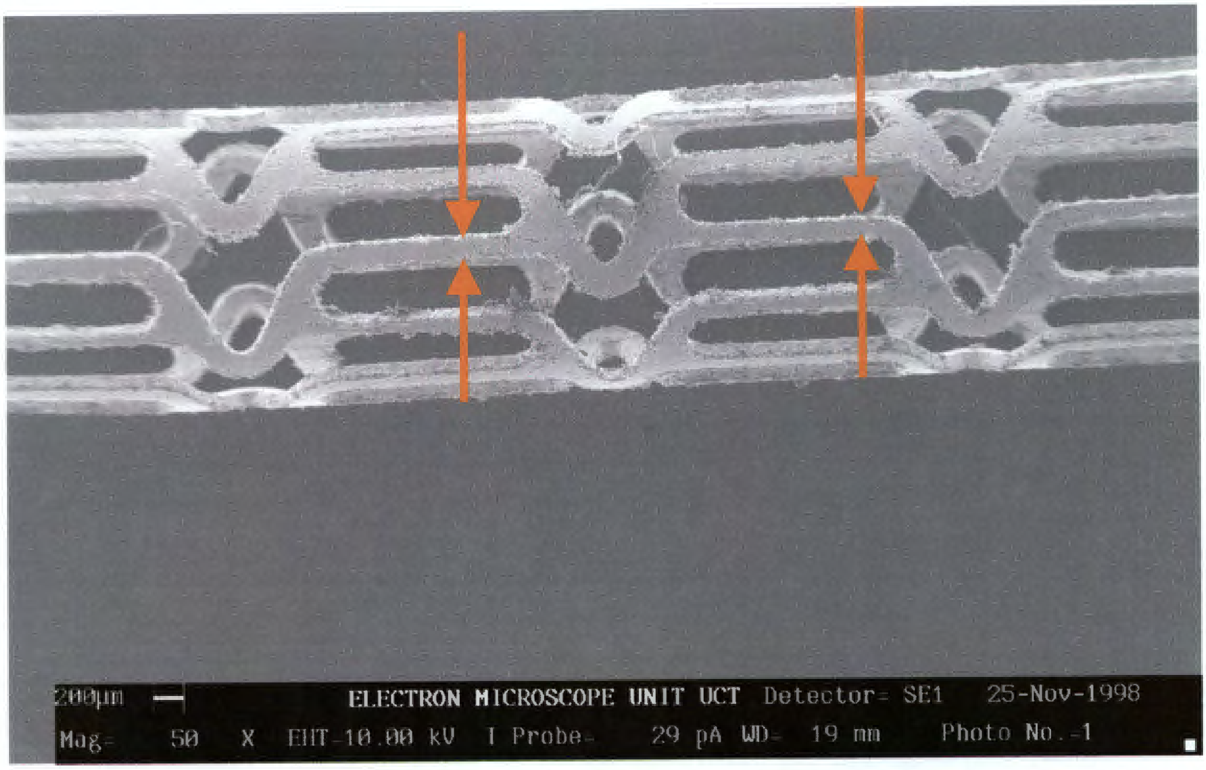


Figure 5.14 *Overall view (50x magnification) SEM image of a spark eroded specimen of the final prototype. Variations in strut width are obvious (arrows).*

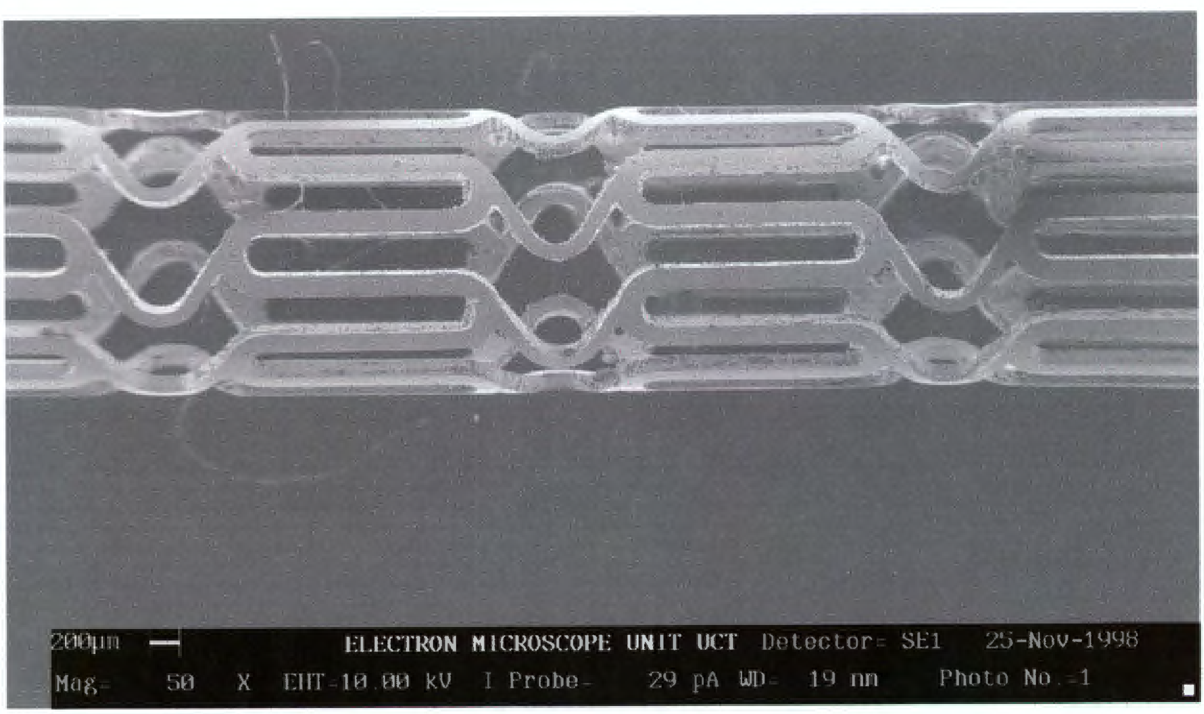


Figure 5.15 *Overall view (50x magnification) SEM image of a laser cut specimen almost similar to the final design. The geometry is very regular.*

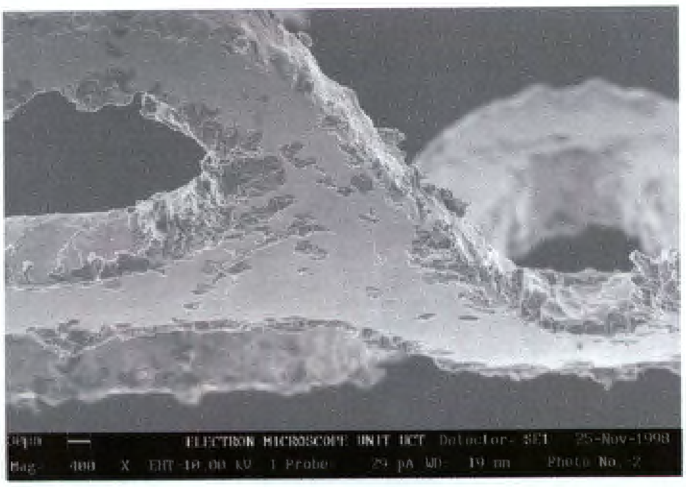


Figure 5.16
Close up view (400x magnification) SEM image of the cutting edges of a spark eroded specimen of the final prototype. Dust and dirt particles have not been removed before scanning but the rough cutting edges and burrs are clearly visible.

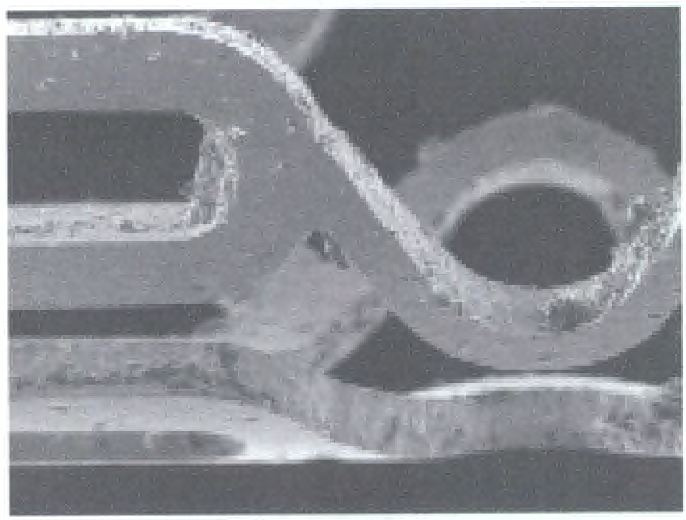


Figure 5.17
Close up view (400x magnification) SEM image of the cutting edges of a laser cut specimen. Dust and dirt particles have not been removed before scanning. Very smooth and burr free cutting edges as compared to the spark eroded stents.

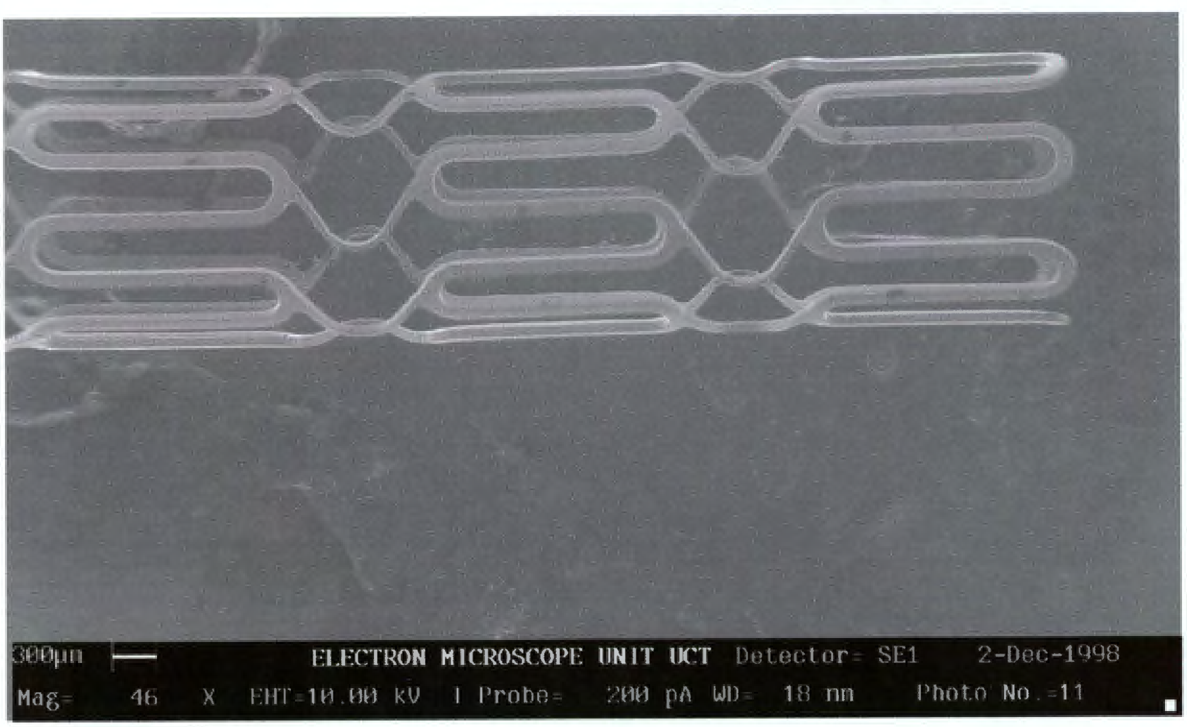


Figure 5.18 A SEM image of a laser cut and electropolished specimen demonstrating the result of state of the art stent manufacturing.

5.5.3 Discussion and Conclusion

The images of the spark eroded stent show that there is significant fine tuning of the manufacturing process necessary in order to achieve acceptable geometrical accuracy. Especially when looked at the results of the finite elements analysis and the critical regions of peak stress compared to the variations in strut width shown in Figure 5.14 it becomes clear that the achieved tolerances in the prototypes is not sufficient.

Chapter Six

Discussion and Recommendations

This thesis reports the evaluation of the present possibility and feasibility of manufacturing coronary stents locally for the South African market. The thesis was divided into three major parts: a review of existing literature and analysis of currently available stents (Chapter 2); the development of a suitable stent structure including its prototyping (Chapters 3 and 4), and a section in which basic design and prototype tests were undertaken (Chapter5).

The initial step of a design or development process is normally the investigation of existing relevant literature and material. A summary of an extensive literature review therefore gives basic information on coronary intervention and coronary stenting in particular, followed by a brief discussion of literature evaluating the technique of coronary stenting.

There is little doubt that PTCA followed by stenting has evolved into the treatment of choice for suitable coronary stenoses. The safety and relative simplicity of coronary stenting and its rising popularity as an effective treatment for many cases of coronary heart disease is well recognised in the literature. This fact, together with the economics of the South African medical device market and the expected increase of coronary heart disease in South African society with its recent lifestyle changes (Sunday Times, 2000), points at this stage to a strong demand for a South African manufactured coronary stent.

The discussion of available design varieties in the subsequent section of the first part ignores the fact that, coronary stents based on the balloon expandable slotted tube design, play a dominant role on the current market. Still, this overview was found to be necessary to complete the picture of coronary stent design and to set the scene for the design process that follows.

Chapter 2 ends with a brief evaluation of the South African patent situation, which should not be regarded as being complete although significant effort was spent to achieve a full coverage. It should merely be seen in the context of the basic message to be extracted. It was found that the technique of vascular stenting and vascular stent implants are apparently not patented – neither nationally nor internationally. However, certain design features of stents are patented, which includes coatings or specially shaped struts. Since these claims are very specialised to a particular feature of a stent, there is little danger of infringing patents with a rather conservative design, especially when it only gets sold on the local market.

The second and core part of this project starts off with the choice of a suitable design concept for the stent before describing its design and prototyping. The method of decision analysis by quantifying certain stent characteristics and comparing them to the demanded requirements is a proven engineering and design tool. Besides the advantages of this method in terms of structuring the decision process, it helps to illustrate and to describe the design process, keeping it transparent and understandable. The choice of the design concept was largely dictated by the manufacturing technique to be used and to a lesser extent by the particular qualities of the individual design concepts. The repetitive, relatively simple pattern of the chosen structure lends itself to design adaptation for spark erosion.

Still, the same decision in favour of the balloon expandable corrugated ring slotted tube design for coronary stents has also been made by the majority of cardiologists world-wide. It turns out to be the design variety of choice for the most popular stents on the market (Serruys *et al.,* 1998). This strong confirmation of the decision made in chapter three therefore is also favourable for meeting one of the goals of this project, which is the introduction of a well proven and accepted design concept to the South African market. As pointed out in the context, doing other than this would have had a negative influence on the rapid acceptance of the product in the local market. A completely different appearance of the new stent would have built up unnecessary barriers. As a result there is no doubt that the designed stent falls within the category of a 'me too' product, but because of its similarity to some existing and exceptionally successful products, it also represents the state-of-the-art in current coronary stent design.

Based on the design concept and the manufacturing technique there was little room for variations of geometrical design parameters. Still, the most important ones were analysed in terms of their possible effects on the stent performance. The outcome was then used to optimise the design for the purpose of this project within the given boundaries. Although significant design refinements were not intended and not purposely achieved, this analysis led to a deeper understanding of design parameters and their potential influence on the stent performance.

Within the group of vascular stents, coronary stents represent the smallest stents in size, as opposed to peripheral stents that reach diameters of up to 14mm. The rationale behind the choice of the smallest stent and therefore the one most difficult to manufacture, was that if these small sizes could be spark eroded to a satisfying quality, adaptation of the design and manufacturing process to larger sizes would not be a great challenge.

Although other manufacturing techniques for slotted tube stents, such as laser cutting and photochemical etching, are also being used, spark erosion was chosen for this project because of its availability. The initial prototypes did indeed look very promising and a significant improvement in quality could soon be achieved. However, the quality of cutting edges at termination of the prototyping phase was by no means suitable to match the present high standards set by laser cutting (Figures 5.14 to 5.17). It is questionable if the spark erosion equipment offered the right range of parameters for sparking the desired structures into a tiny tube. There is no doubt that the achievement of smoother cutting edges is dependent on low values for the discharge energy, which was set to the lowest value for our experiment. The prototyping therefore was terminated with the understanding that the necessary low discharge energy would increase the already excessively long manufacturing time of 2.5 hours per stent even further. During the prototyping phase of the project the emphasis was placed on a satisfying result of the spark erosion process in terms of surface quality at cutting edges and the achievement of an acceptable overall geometry.

The fulfilment of the necessary tight tolerances would have involved subsequent extensive detail work on the sparking electrodes with additional cost involved. Because the quality of the stents manufactured by the spark erosion technique continued to be unsatisfactory, this point was deemed to be of secondary importance. An extensive fine-tuning for achievable tolerances has therefore not been performed.

The resulting final prototypes are not suitable for use, *in vivo*, although their design was subjected to basic testing. Besides the geometrical irregularities that were still present in the final prototypes it must be noted that the stents were not electropolished which could have influenced their mechanical properties. The tested prototypes do not represent the exact geometry of the drawn up design that was for instance used in the computer simulation of deployment. For this reason, an exact quantitative evaluation and estimation of standard deviations and measurements was neglected. The focus was rather concentrated on qualitative results and deformation characteristics.

The computational analysis of the deformation properties of the stent using the finite element method demonstrates a possible application of the technique to the stent structure design and points out typical critical areas of deformation. It was concluded that these critical areas must be given particular attention when allowing for manufacturing tolerances. The analysis also illustrates the deployment process. These results could serve as the basis for a subsequent and more refined design.

The electron microscopy images clearly show the discrepancy between state-of-the-art surface quality obtained by laser cutting and the spark erosion of the final prototypes. As mentioned previously, significant improvement of this feature would have involved much longer manufacturing times and again this casts some doubt on the suitability of the range of possible settings of the spark erosion machine.

Although the outcome of the experimental manufacture of the final prototypes by spark erosion demonstrates the principal suitability of the technique for a common design variety, the actual result of this project must be looked at from a different perspective. The prototyping phase was suspended when it was clear that the cost of manufacture of the coronary stent with the spark erosion equipment used would exceed the cost of laser cutting by far. Although detailed costing estimates were initially not part of this engineering-based project, it is instructive to report the quotations received from laser cutters in Europe. Laser cutting for one item accounts, depending on the cut volumes, for the cost of operating the spark erosion machine used for this project for less than one hour. Considering the time of more than 2.5 hours used to spark erode one of the final prototypes, and the expected increase in manufacturing time to achieve the necessary improvement in quality, the evaluated manufacturing technique is obviously uneconomic. Therefore, the spark erosion technique must be considered to be unsuitable within the broader context of providing the South African market with an economical coronary stent.

A final point to be addressed is the possible set-up of laser cutting for stent manufacture in South Africa. Depending on the level of automation, the cost for a suitable laser cutting machine would exceed R 1million. A roughly estimated total number exceeding 10,000 stents would need to be cut to make the investment of such equipment feasible. The total demand for coronary stents in South Africa in

2000 is expected to exceed 6,000 stents (Starke, 1999). Facing a very competitive market, a South African designed stent would cover only a fraction of this. On the other hand, there is a rising new market for peripheral stents. Although reliable data cannot be provided at this stage, by looking at the volumes of stents in demand for the local market versus the cost of established laser cutting equipment and expertise, it would take several years to achieve the necessary volumes. Still, considering all those factors, the set-up of stent manufacturing in South Africa might be feasible in the future.

Although the project failed to prove the feasibility of the proposed manufacturing technique for a coronary stent, the demonstrated approach for design and testing does form the basis for further development of a variety of stents for the South African market. The actual result that subcontracted laser cutting is an economical way of manufacturing a stent even for the local market, leaves open the possibility for a range of design improvements. For example, it is not necessary to have a repetitive pattern of similar opening along the longitudinal axis. Also, the list of stent properties determined by the mechanical design is certainly longer than mentioned here but taking them into account would not have contributed to the main purpose of the project in hand. Especially with the use of tools such as the finite element analysis, the influence of certain design parameters on radial strength, longitudinal flexibility or secure crimpability of the stent structure can be more closely examined and detailed design improvements could be effected. A possible follow-up to this project could therefore be the in-depth design optimisation of the stent structure based on manufacturing by laser cutting.

APPENDIX A

PATENT ABSTRACTS

The South African Patents 94/0334 and 94/3522 protect particular stent design features or manufacturing methods as described in their illustrated abstracts (Figure A1 and A2).

21: 94/0334. 22: 1994-01-18. 43: 95-07-18.
51: A 61 F.
71: Schneider (USA) Inc.
72: David W. Mayer.
33: US. 31: 08/006,216. 32: 1993-01-19.
54: **Clad composite stent.**
00: 35.

1995 -09- 2 7

57: A body compatible stent (16) is formed of multiple filaments (18,20) arranged in two sets of oppositely directed helical windings interwoven with one another in a braided configuration. Each of the filaments (18,20) is a composite including a central core (24) and a case (26) surrounduing the core (24). The outer case (26) is formed of a relatively resilient material, e.g. a cobalt/chromium based alloy. The composite filaments (18a) are formed by a drawn filled tubing process in which the core (24) is inserted into a tubular case (26) of a diameter substantially more than the intended final filament diameter. The composite filament (18a) is cold-worked in several steps to reduce its diameter, and annealed between successive coldworking steps. After the final cold working step, the composite filament (18a) is formed into the desire shape and age hardened.

1/2

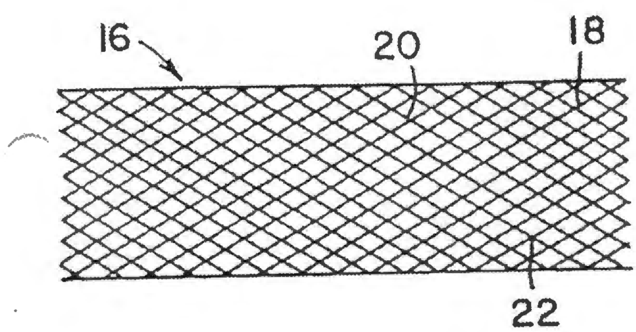


Figure A1 Patent abstract of a manufacturing method for stents made out of wire filaments

21: 94/3522. 22: 20 May 1994. 43: 95-01-23.
51: A 61 B. 1995 -03- 28
71: A. Bromberg & Co. Ltd.
72: Josef Flomenblit; Nathaly Budigina; Yuval Bromberg.
33: IL. 31: 105828. 32: 28 May 1993.
54: **Medical stent.**
00: 22.

57: A stent for placing in a tubular organ so as to support its diameter to remain above a critical diameter. The stent comprises a spiral coil or cylinder made of a two-way shape memory alloy and has a super-elastic state in which the stent's diameter is at least about the critical diameter or more but within a physiological range tolerated by the organ and having a soft state in which the stent's diameter, after changing to this state from the super-elastic state, which is less than the critical diameter. The shape memory alloy has two transition temperatures being within a range that will not damage biological tissue, of which a first transition temperature is a temperature in which it changes from the soft state to the super-elastic state and of which a second transition temperature is a temperature in which it changes from the super-elastic state to the soft state. The arrangement being such that after changing into one of the two states, the stent remains in that state at body temperature.

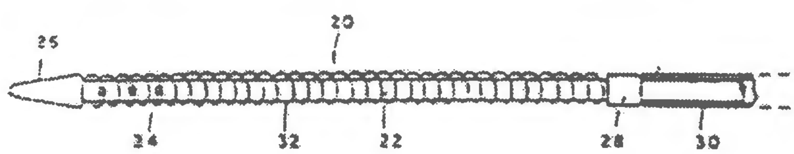
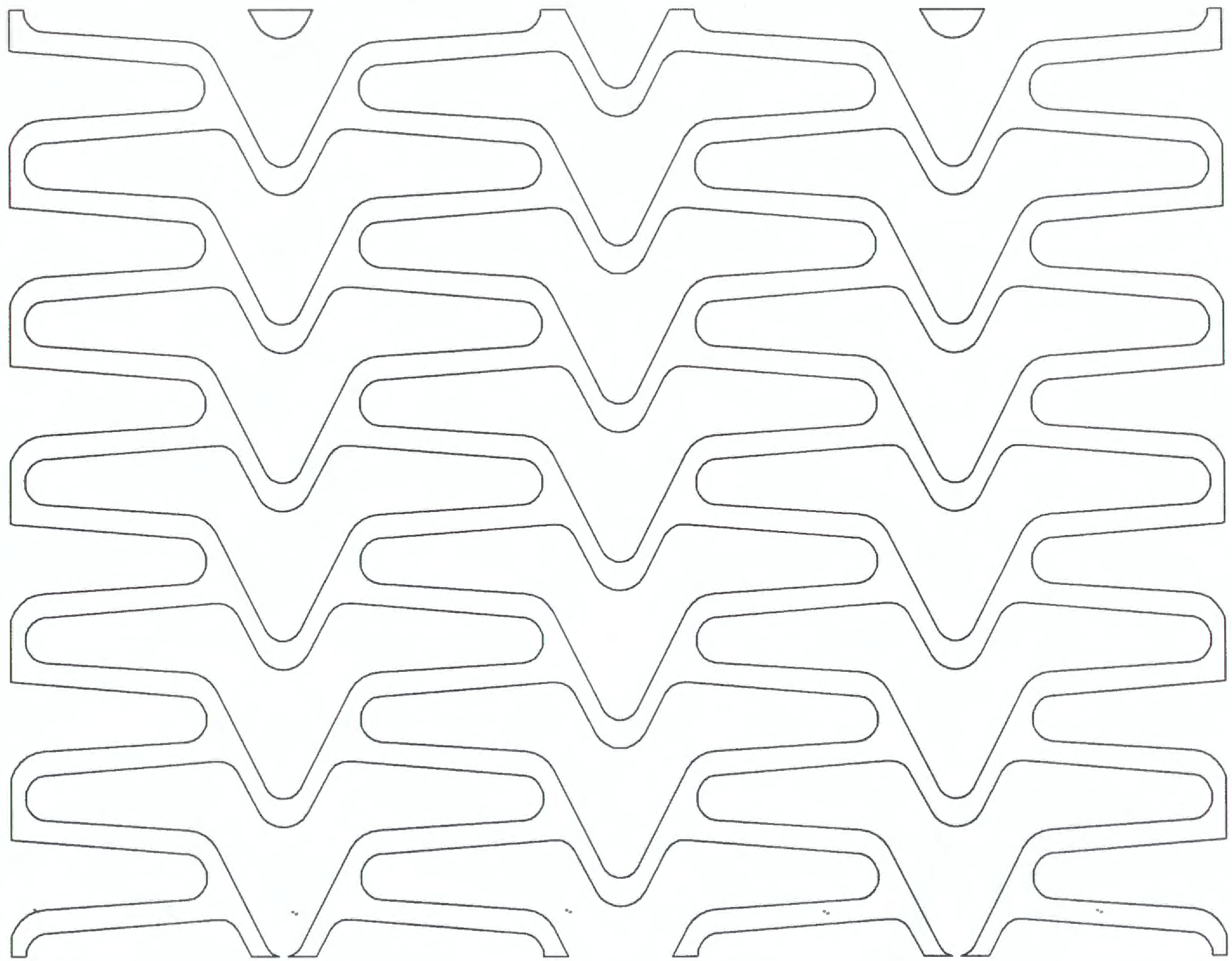


Figure A2 Patent abstract of a shape memory stent.

Appendix B

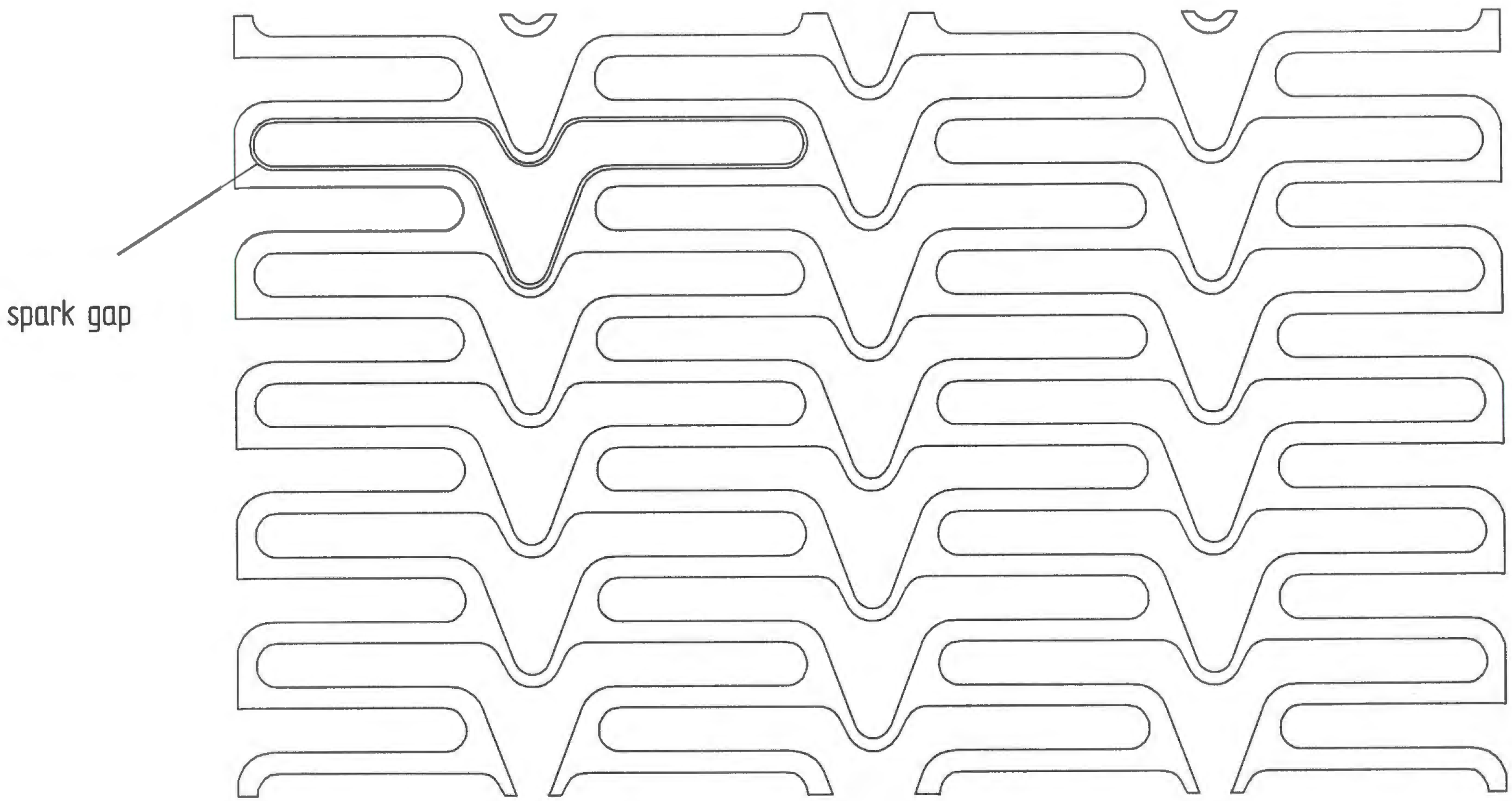
Technical Drawings

*Dimensions for electrodes and stents are contained in *.dxf files

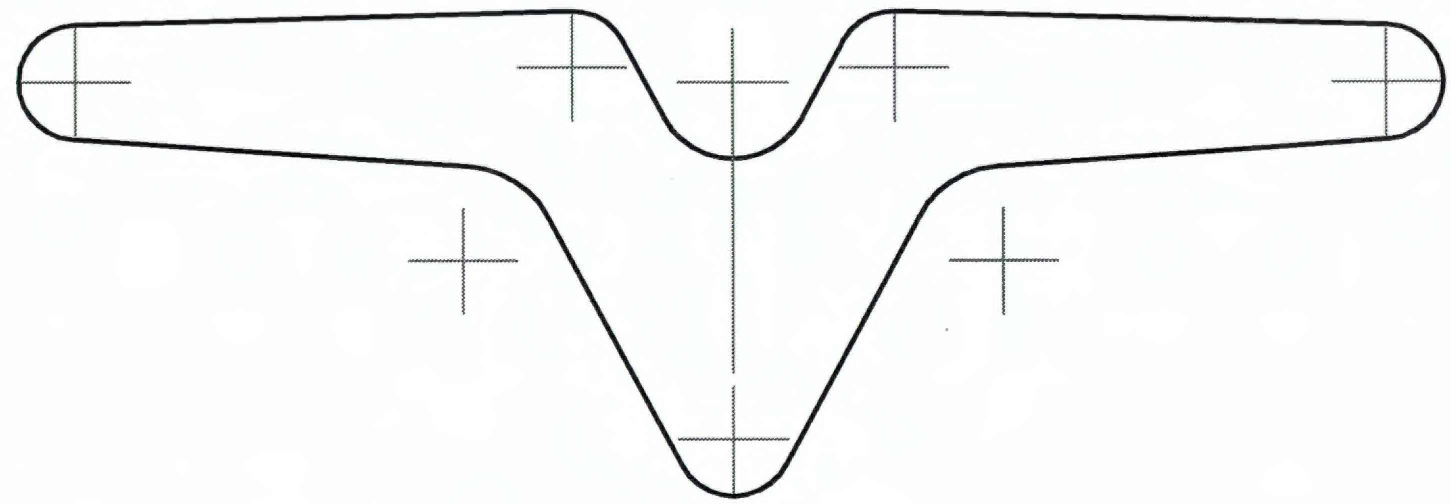


20:1 (scale)	+0.02 (tolerances)	SS316L				

Coronary Stent for the South African Market	**Stent** (assembly)		
	Initial Prototype (name)	(date)	page 1 of 1



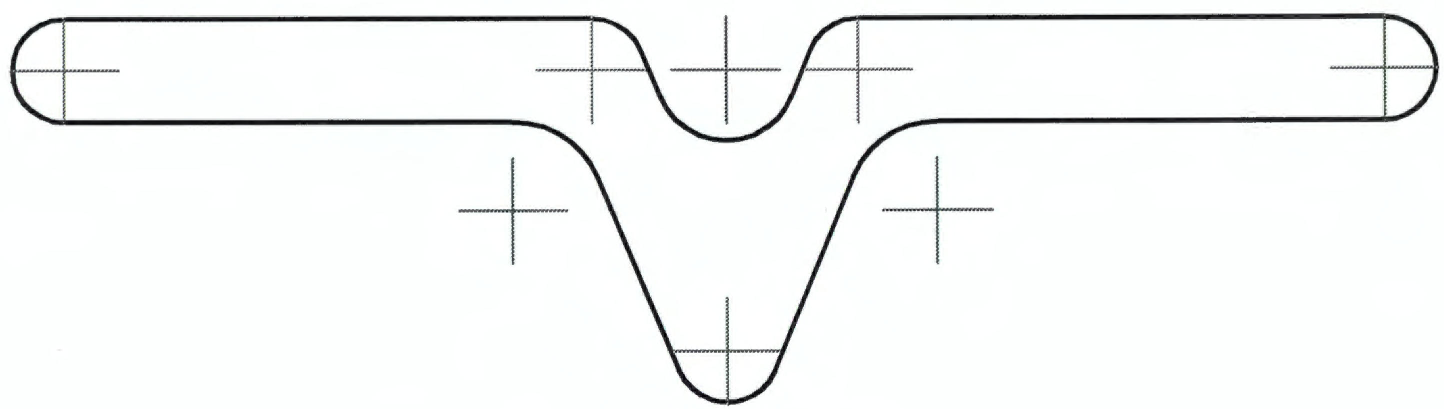
scale 20:1	tolerances +0.02	SS316L				
Coronary Stent for the South African Market		assembly Stent				
		name Final Prototype			date	page 1 of 1



.dxf file for programming of wire erosion

50:1 (scale)	+/-0.02 (tolerances)	KE-Cu				

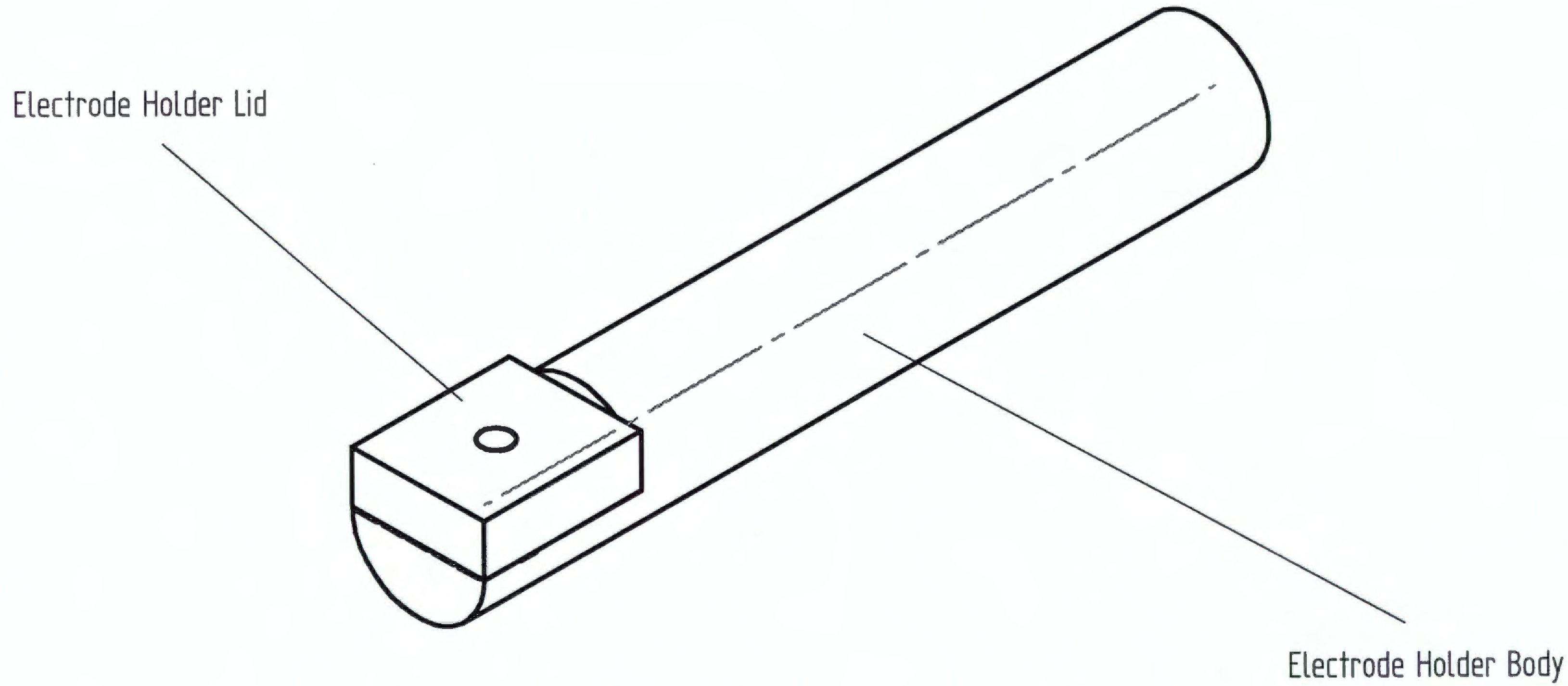
Coronary Stent for the South African Market	**Electrodes** (assembly)		
	Electrode for Initial Prototype (name)	(date)	page 1 of 1



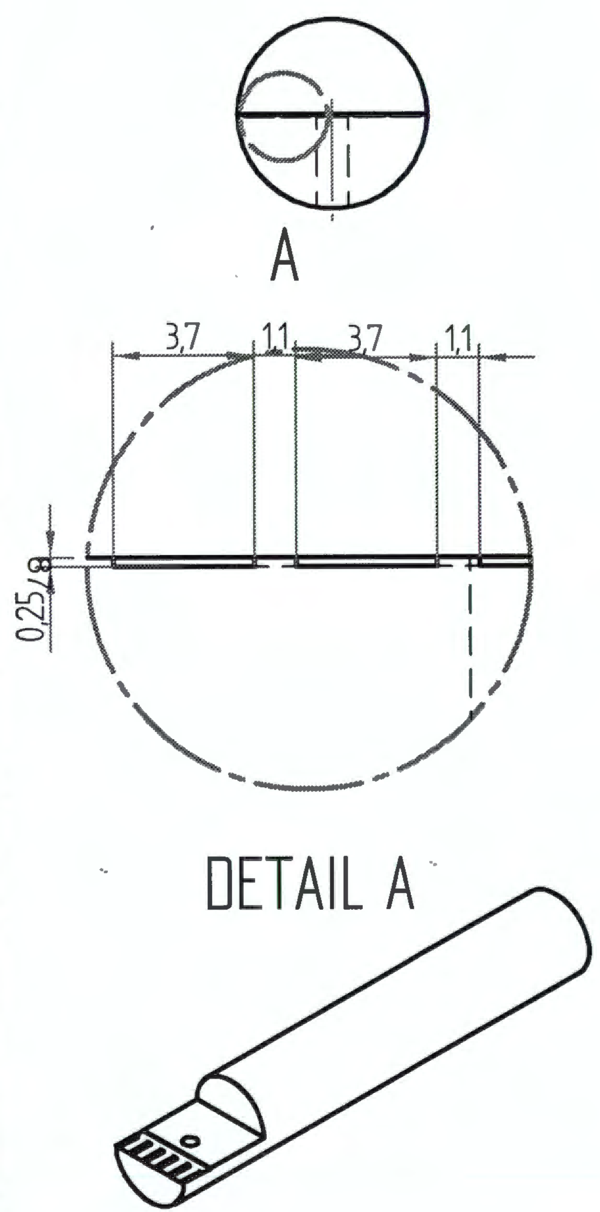
.dxf file for programming of wire erosion

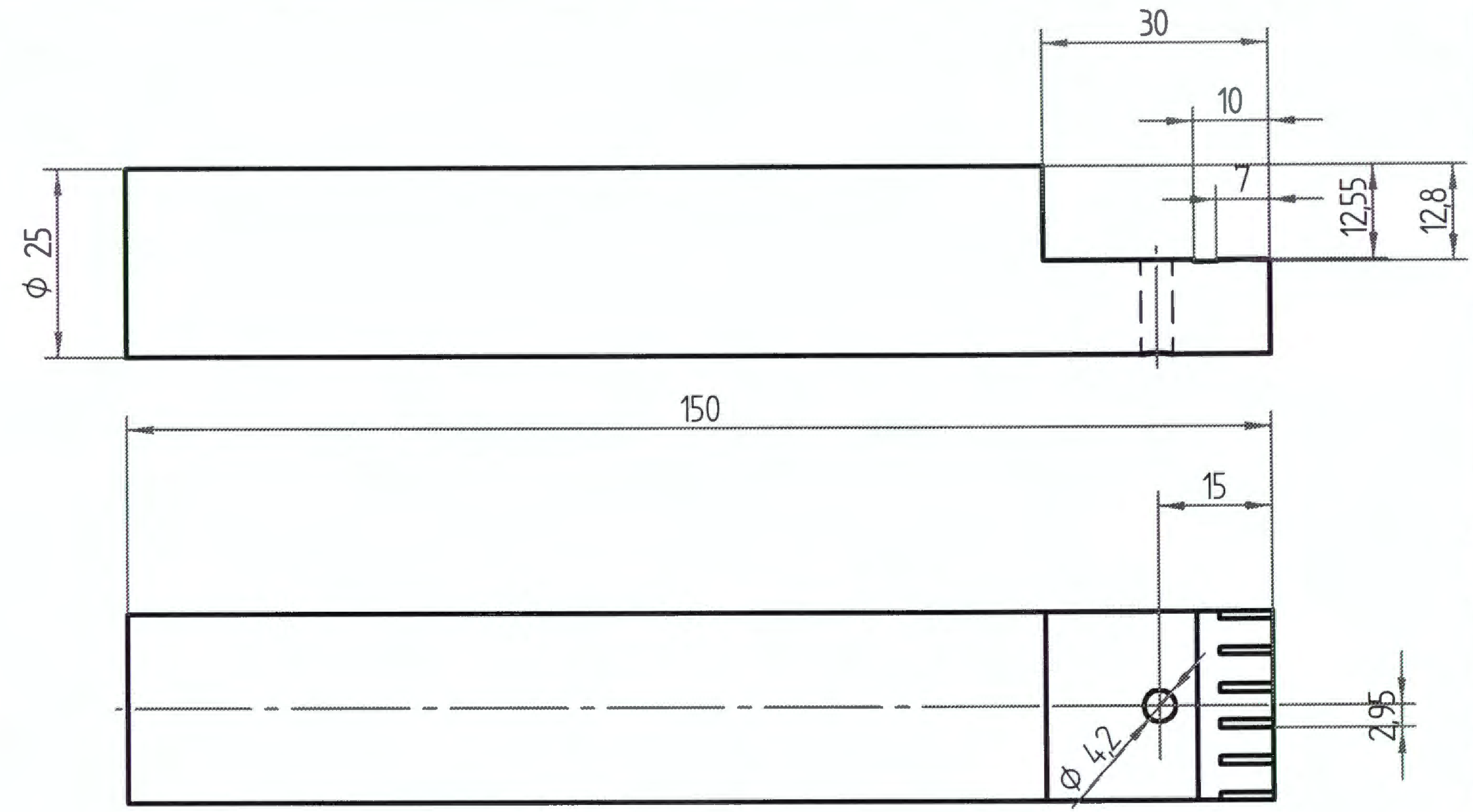
50:1 (scale)	+/-0.02 (tolerances)	KE-Cu				

Coronary Stent for the South African Market	**Electrodes** (assembly)		
	Electrode for Final Prototype (name)	(date)	page 1 of 1

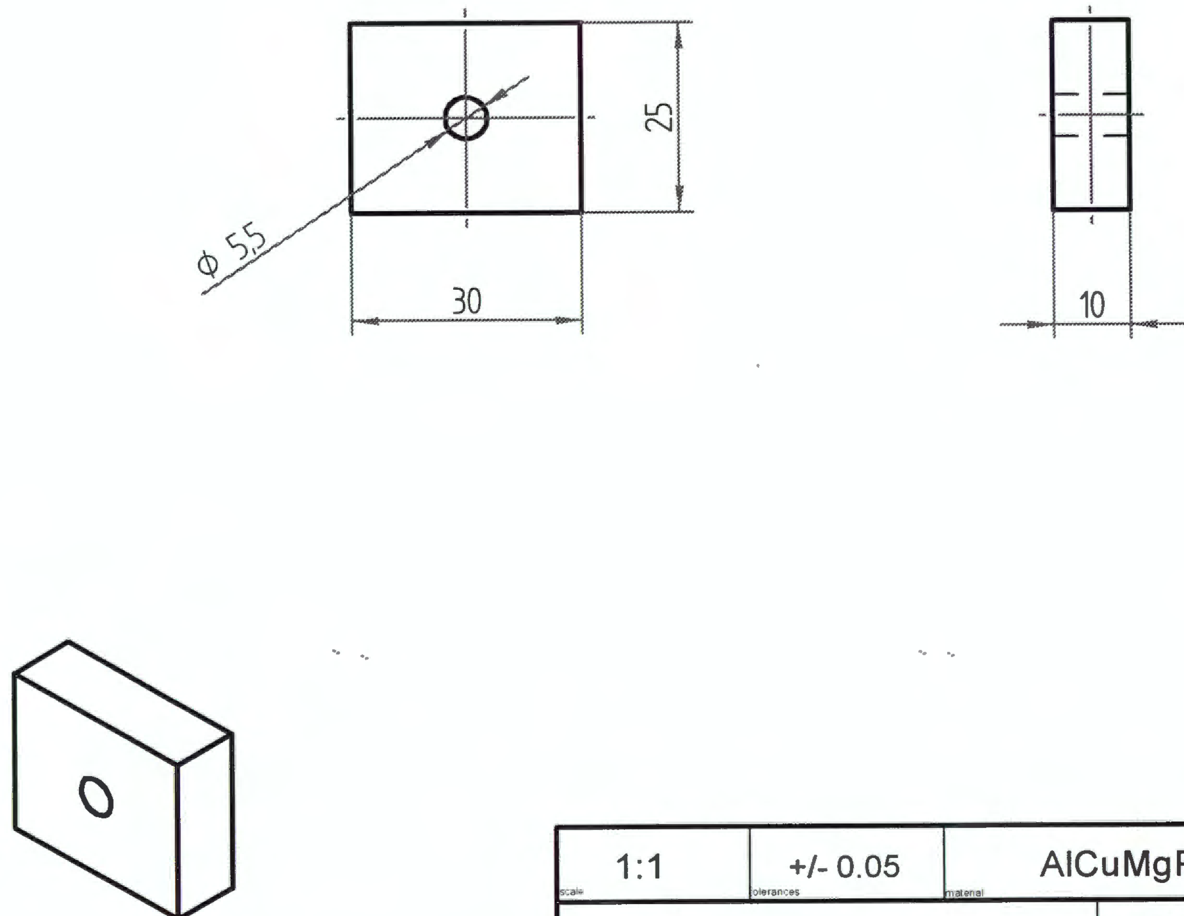


1:1						
Coronary Stent for the South African Market	**Tools and Appliances: Electrode Holder**					
	Electrode Holder Assembly					page 1 of 3



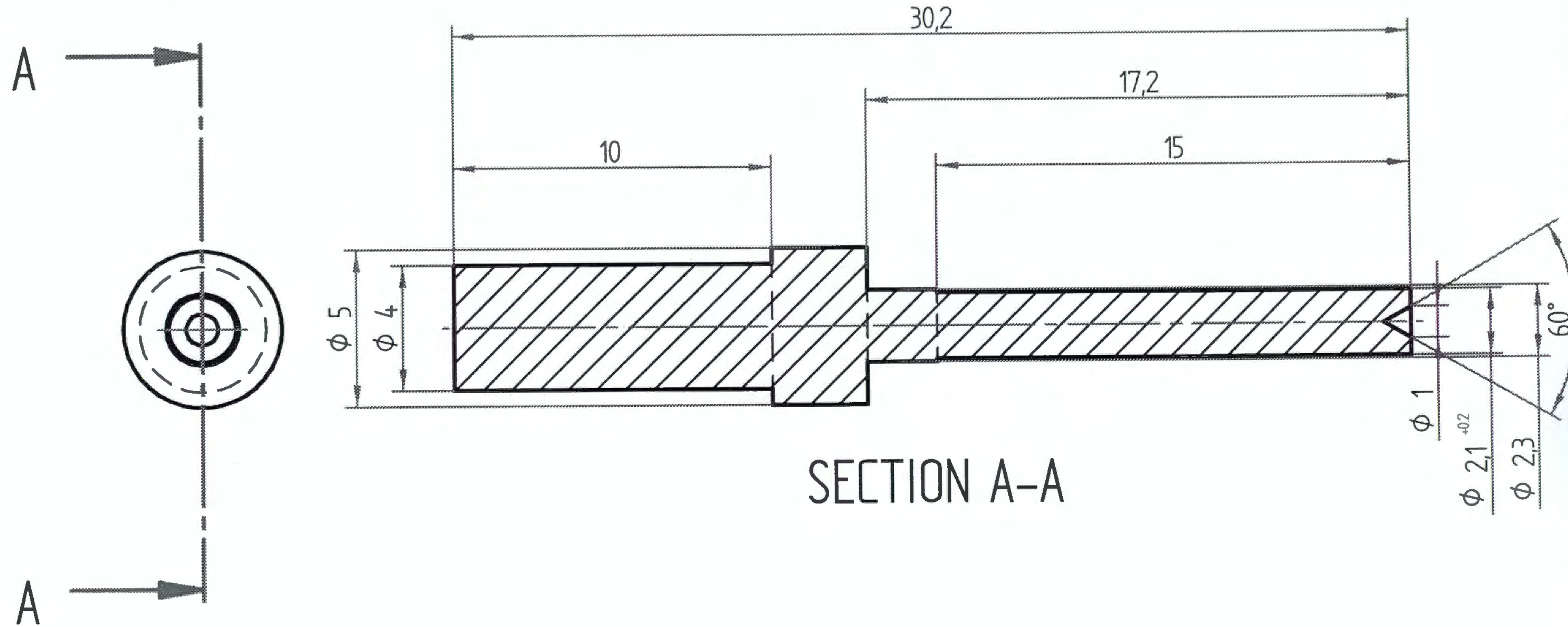


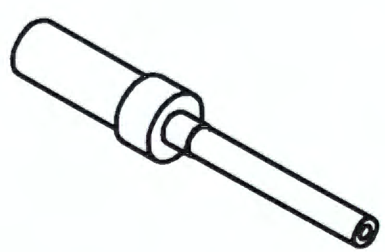
scale 1:1	tolerances +/- 0.05	material AlCuMgPb				
Coronary Stent for the South African Market		assembly Tools and Appliances: Electrode Holder				
		name Electrode Holder Body		date		page 2 of 3



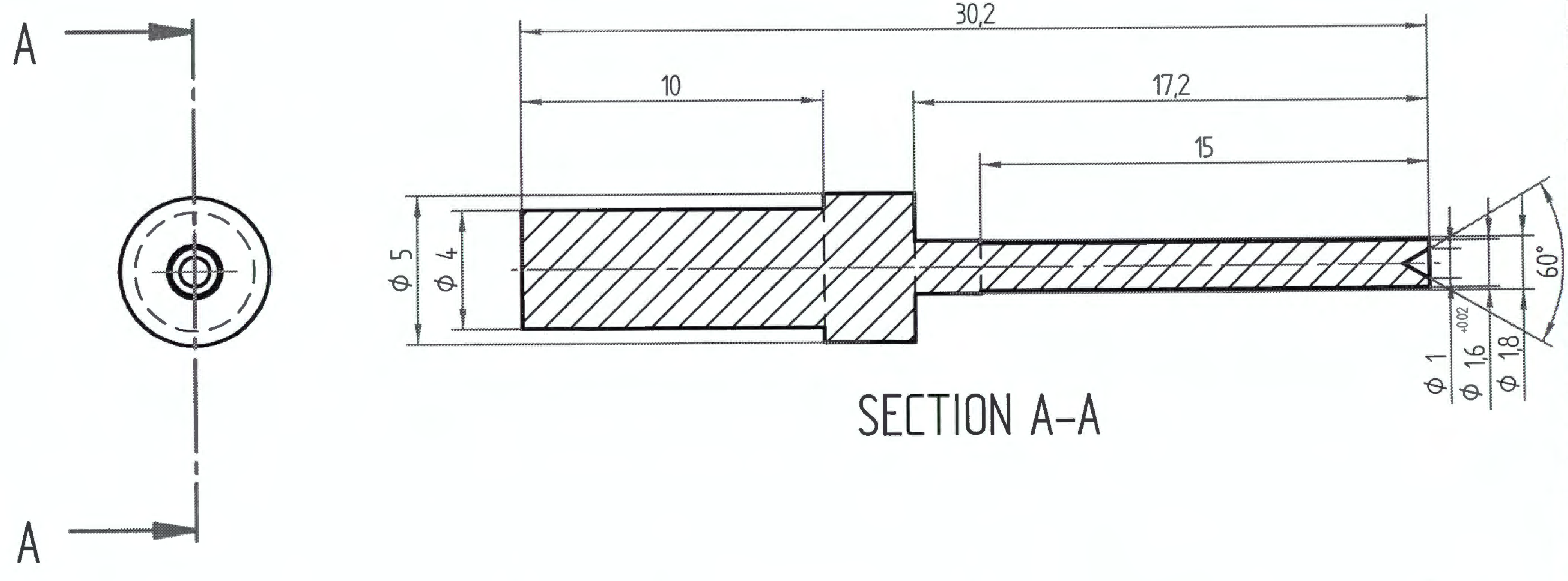
1:1 (scale)	+/- 0.05 (tolerances)	AlCuMgPb (material)				

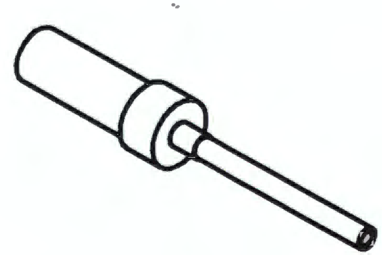
Coronary Stent for the South African Market	**Tools and Appliances: Electrode Holder** (assembly)		
	Electrode Holder Lid (name)	(date)	page 3 of 3



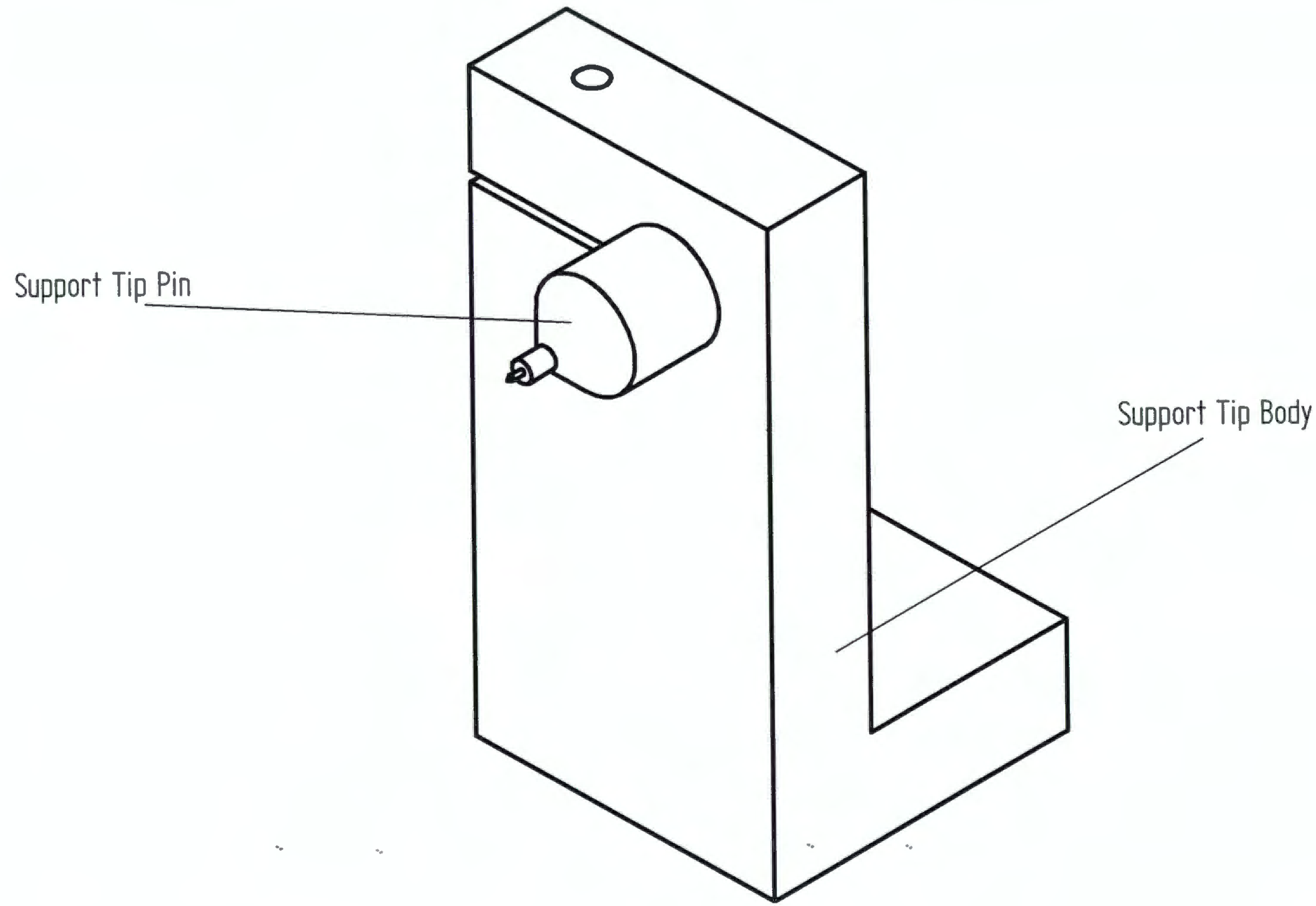


scale	tolerances					
5:1	+/-0.05	AlCuMgPb				
Coronary Stent for the South African Market	assembly: **Tools and Appliances: Supp. Appliances**					
	name: Support Pin for Initial Prototype		date	page 1 of 1		

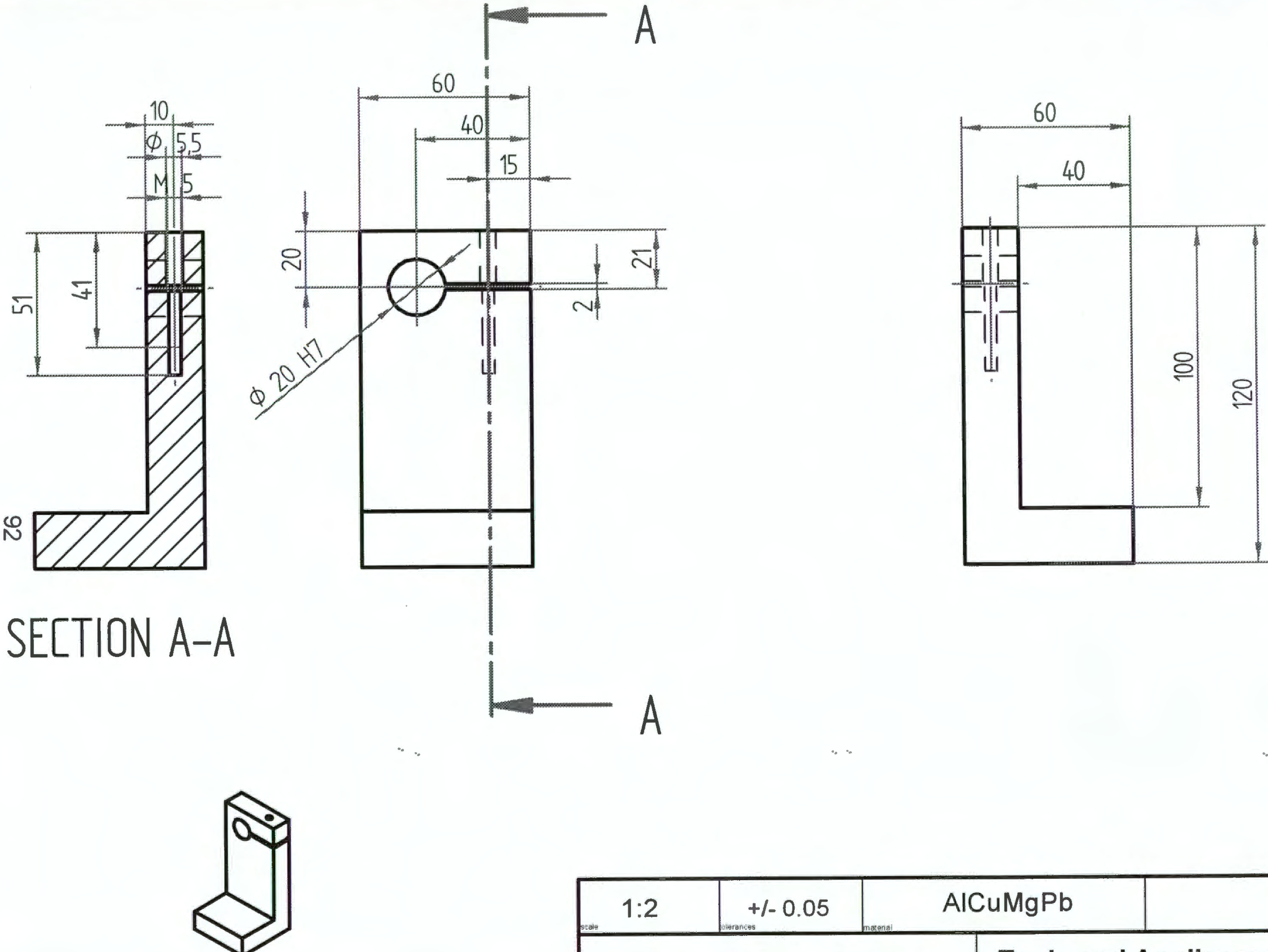




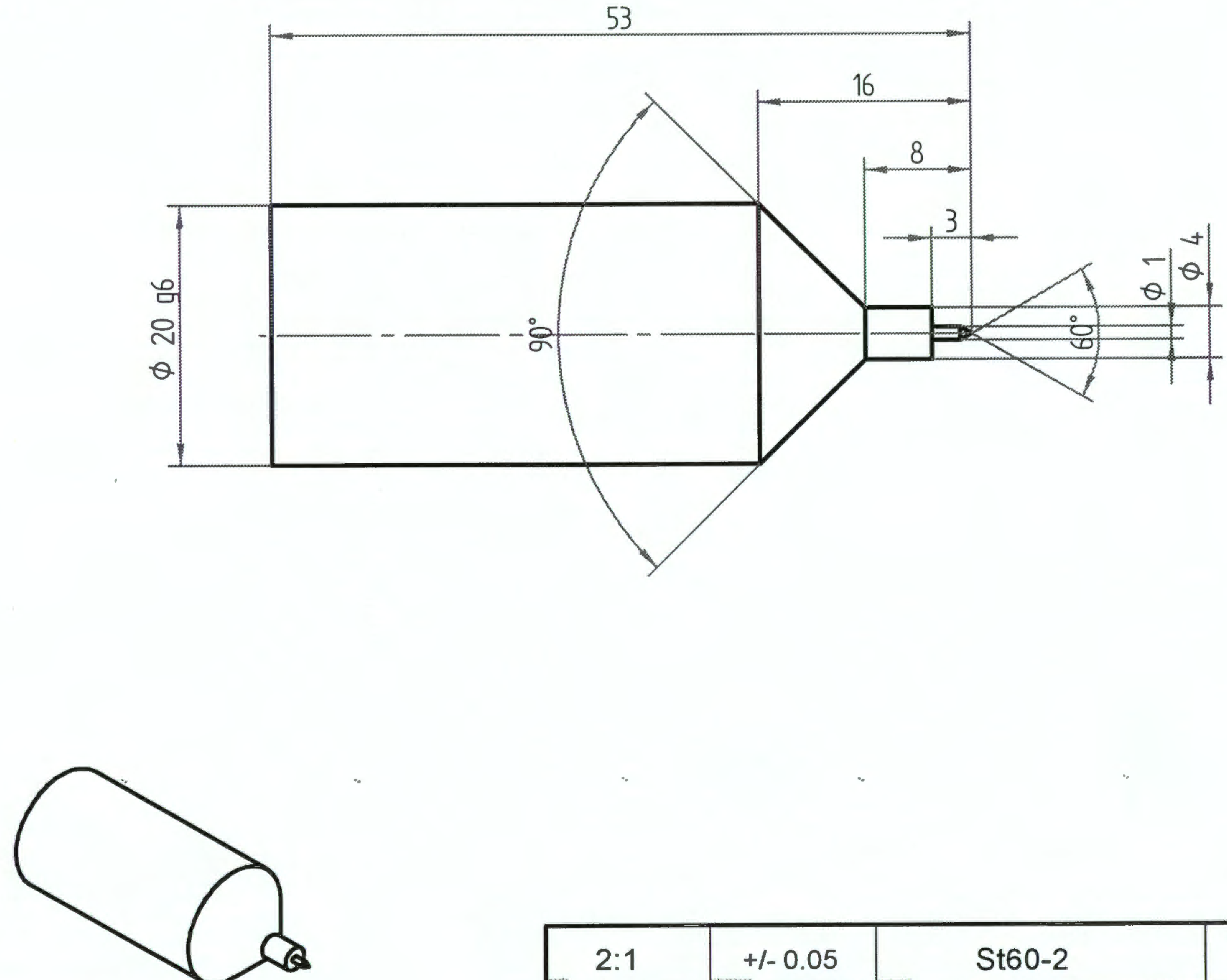
5:1 (scale)	+/-0.05 (tolerances)	AlCuMgPb				
Coronary Stent for the South African Market			**Tools and Appliances: Supp. Appliances** (assembly)			
			Support Pin for Final Prototype (name)		(date)	page 1 of 1



scale 1:1	tolerances	material
Coronary Stent for the South African Market	assembly **Tools and Appliances: Support Tip**	
	name Support Tip Assembly	date / page 1 of 3



scale 1:2	tolerances +/- 0.05	material AlCuMgPb				
Coronary Stent for the South African Market	assembly **Tools and Appliances: Support Tip**					
	name Support Tip Body			date	page 2 of 3	



2:1 (scale)	+/- 0.05 (tolerances)	St60-2 (material)				
Coronary Stent for the South African Market	**Tools and Appliances: Support Tip** (assembly)					
	Support Tip Pin (name)	(date)	page 3 of 3			

APPENDIX C

MANUAL FOR THE MANUFACTURE OF A CORONARY STENT

This manual was handed to the spark erosion machine operator to manufacture a number of prototypes for testing purposes.

MANUAL FOR THE MANUFACTURING OF A CORONARY STENT

1. Preparation of the Spark Erosion Machine

1.1 Mounting of the Indexing Head to the table of the spark erosion machine:

The rotation axis of the indexing head must be in line with the x-axis of the spark erosion machine table. Align the indexing head by mounting a straight pin into it and adjust it using a micrometer clock while moving the table in x-direction.

1.2 Operating Parameters

Set the parameters for the sparking process according to the table.

End value	-0.600mm
On time	2ms
Off time	1ms
Spark time	2s
Flush time	1s
Current	0.5A
HV (voltage range)	1
Zapper (waveform)	1
Servo	5
Gap	2
Arc	0

Table C1: Values for operating parameters

1.3 Preparation of the Electrode Holder

- Ensure that the electrodes are straight and free of burrs.
- Mount the electrodes into the electode holder, allowing them to stick out about 3.5mm.

- Machine the electrodes to an equal length of about 3mm. A small cutter (<10mm diameter) and high rpm are required. Do not cut more than 0.1mm at a time!
- Carefully deburr the tips of the electrodes.
- Check if electrodes are still straight and in line.
- Mount the electrode holder to the ram of the spark erosion machine and align the row of electrodes to the x-axis of the machine table.
- Machnine the tips of the electrodes after every stent sparked.

2. Mounting of the Tube

- push the tube over the small diameter of the support pin until it comes to lie against the shoulder to the next bigger diameter. Ensure that the tube is pushed on completely and there are no burrs or debris creating a gap between the tube and the shoulder 2 (Figure C1). The tube on the pin must have a tight fit.
- Mount the pin with the tube into the clamping ring of the indexing head.
- Introduce the support tip to the free end of the pin
- rotate the indexing head while clocking the cyclic running of the tube/ pin assembly with a micrometer clock. Adjust the tip until a running deviation of +/- 0.001mm is reached. Tube/ pin assemblies where this deviation cannot be achieved must not be used.

3. Positioning of the Electrodes

The electrode assembly needs to be positioned correctly relative to the stent.

- X-axis:

  Move the machine table in negative x-direction until the outer electrode touches the shoulder of the large diameter of the support pin (Figure 2). Set the value for the x co-ordinate of the table to x=-2410mm. Move the table to x=0mm.
- Y-axis:

  Position the middle of the electrodes to the rotation axis of the pin. Therefore move the table into negative y-direction until the electrodes touch the tube (Figure

3). Set the value for the y-coordinate of the table to y=+1.400mm. lift the ram and move the table to y=0mm.

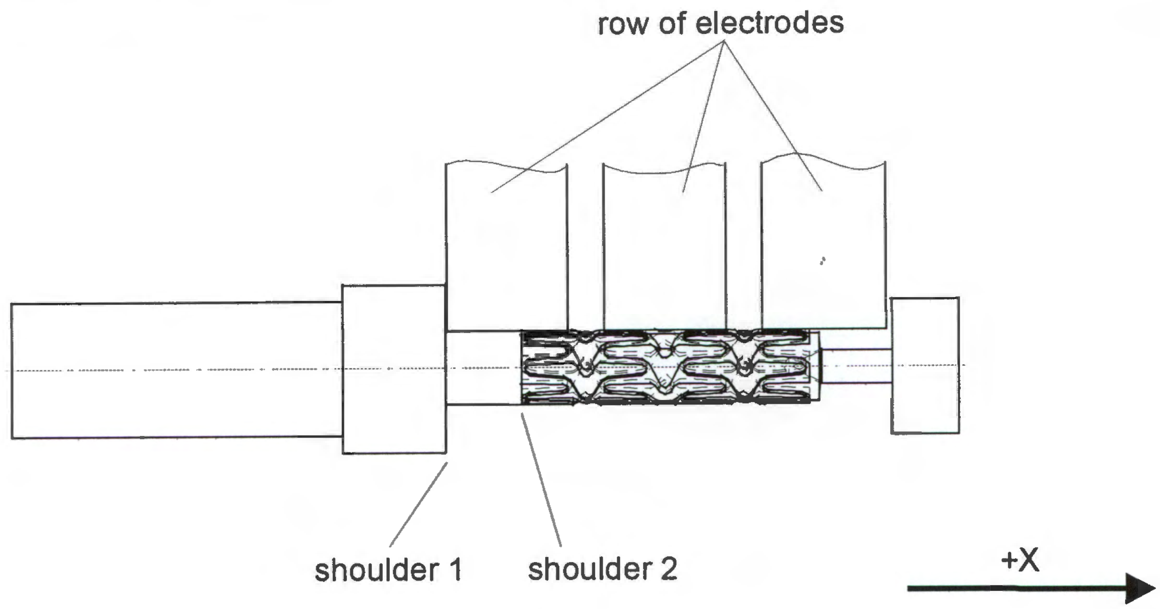


Figure C1 *The outer electrode touches the shoulder of the large diameter of the support pin.*

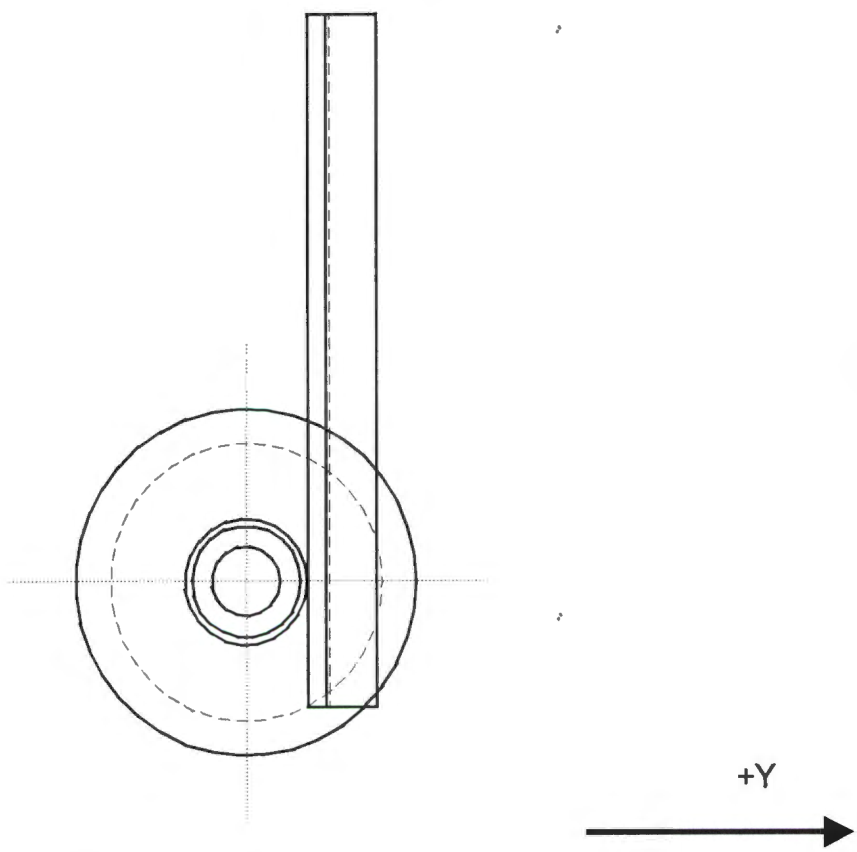


Figure C2 *The row of electrodes must touch the tube.*

- Z-axis:

  Drive the ram down until the tips of the electrodes touch the pin. Set the value for the z co-ordinate to z=0.

4. Sparking

- Position the indexing head on 0^0.
- Make sure that the machining parameters are set correctly (see 1.)
- flood the table with dielectric fluid and start sparking. The machine will switch off when the first row of openings is sparked.
- Turn the indexing head. It is important that the rows are sparked according to the given sequence. Spark 6 rows of struts around the circumference at the following positions:
  1. 0^0
  2. 180^0
  3. 60^0
  4. 240^0
  5. 120^0
  6. 360^0
- Move the machine table to x=-2.400mm. Spark 6 rows of struts around the circumference at the following positions:
  7. 330^0
  8. 150^0
  9. 30^0
  10. 210^0
  11. 90^0
  12. 270^0
- Remove the stent/ pin assembly from the indexing head and carefully pull the stent off the support pin.

APPENDIX D

INPUT DECK FOR A FINITE ELEMENT ANALYSIS

The following input deck was entered for the performed Finite Element Analysis of stent deployment. The element and node files are kept separate and are not shown here.

Input Deck	Comment
** JOB...............Analysis of a coronary stent ** ** MODEL.............Balloon deployment ** ** DESIGN............Stent final design ** Diameter = 1.7mm ** Length = 8.7mm ** ** PARAMETERS........Elastic/Plastic Stainless steel ** 3.5mm Rigid surface "vessel" ** 5 Atm Deployment ** ** DATE..............July 1998 ** ---	*Description*
*HEADING One Step Balloon deployment with rigid vessel *PREPRINT,MODEL=YES,ECHO=NO,HISTORY=NO ** Read separate Node File *NODE,NSET=ALL,SYSTEM=C,INPUT=stent_2.cyl *TRANSFORM,TYPE=C,NSET=ALL 0.0, 0.0, -5.0, 0.0, 0.0, 5.0 ** Read separate Element File *ELEMENT,TYPE=S4,ELSET=SS316L,INPUT=stent_2.elm ** ---	*Definition of nodes.* *Transformation into cylindrical coordinates (wrapping of the stent surface into a cylinder)* *Definition of elements and type of elements (S4).* *(The nodes and elements are not listed here)*
** NODES FOR AXIAL SYMMETRY & OUTPUT ** --- *NSET, NSET=SYMM 660, 665, 670, 1635, 1640, 1645, 2610, 2615, 2620, 3585, 3590, 3595, 4560, 4565, 4570, 5535, 5540, 5545 *NSET, NSET=OUTPUT 5734, 66, 241, 349, 5416, 5545	*Grouping of nodes for boundary conditions and output.*

** --- ** MPC FOR ENDS WHICH MEET AFTER CYLINDRICAL WRAP ** --- *MPC TIE, 5770, 943 TIE, 5764, 945 TIE, 5758, 948 TIE, 5752, 951 TIE, 5746, 954 ** TIE, 5406, 722 TIE, 5398, 721 TIE, 5390, 720 TIE, 5382, 719 TIE, 5374, 718 TIE, 5366, 717 TIE, 5358, 716	*Tying up of contact nodes after wrapping of the surface.*
** --- ** SS316L MATERIAL DEFINITION ** --- *SHELL SECTION, ELSET=SS316L, MATERIAL=SS316L 0.1, 3 *MATERIAL, NAME=SS316L *ELASTIC, TYPE=ISO 190.0E3, 0.3 *PLASTIC 170.00, 0.0 679.00, 0.33	*Definition of shell elements with a thickness of 0.1 and 3 nodes throughout the thickness.*
** --- ** CONTACT BETWEEN STENT AND RIGID VESSEL ** --- *RIGID SURFACE, TYPE=REVOLUTION, NAME=VESSEL, REF NODE=9999 0.0, 0.0, -2.5, 0.0, 0.0, 2.5 START, 1.75, 0.0 LINE, 1.75, 5.0	*Definition of the rigid vessel around the stent with 3.5mm diameter*
*SURFACE DEFINITION, NAME=STENT SS316L, SPOS *CONTACT PAIR, INTERACTION=SIMPLE, SMALL SLIDING STENT, VESSEL *SURFACE INTERACTION, NAME=SIMPLE	*Definition of surface properties of stent and vessel.* *Friction free interaction of the stent with the vessel.*

<table>
<tr>
<td>
<pre>
** ---
** SYMMETRY, ROTATIONAL CONSTRAINT & RIGID
SURFACE
** ---
*BOUNDARY
SYMM, 3, 3
SYMM, 5, 5
**
 670, 2, 2
1645, 2, 2
2620, 2, 2
3595, 2, 2
4570, 2, 2
5545, 2, 2
**
9999, 1, 6
** ---
** PRESSURE ON INNER FACE
** ---
*STEP, NLGEOM, INC=1000
*STATIC
0.05, 1.0
*DLOAD, OP=NEW
SS316L, P, 0.5
**
*PRINT,CONTACT=YES
*EL PRINT, FREQ=0
*NODE PRINT, FREQ=0
*RESTART,WRITE, FREQ=20
*NODE FILE, NSET=OUTPUT
U
*END STEP
</pre>
</td>
<td>
Definition of boundary constraints for the stent and the surface (see Figure D1).

Application of pressure (0.5Mpa).

Output format
</td>
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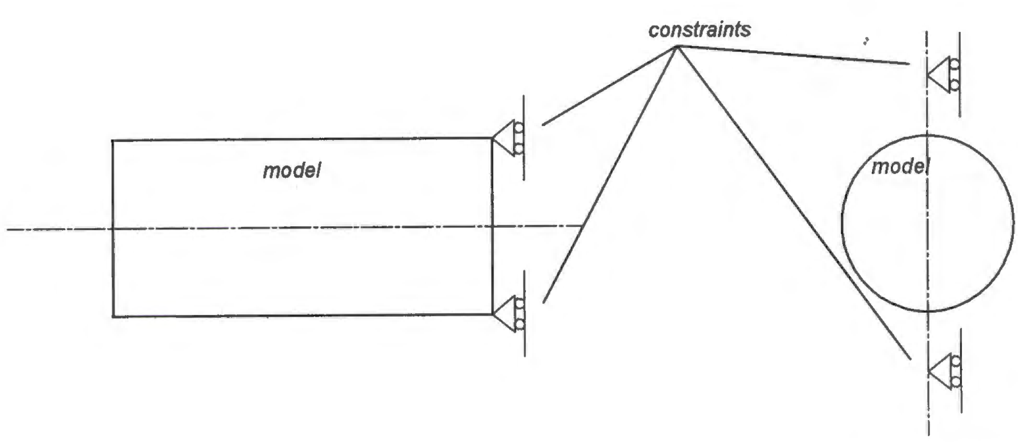

Figure D1 *Boundary constraints restricting translation and rotation of the model.*

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