Cycle-to-Cycle Control of the Angioplasty Balloon Fabrication Process

Dominic Lalli

Department of Electrical and Computer Engineering
Centre for Intelligent Machines – Systems and Control Group
Industrial Automation Lab
McGill University, Montreal, Canada
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Abstract

The development of a new angioplasty balloon from a new material can be a long and arduous process that may take months. These balloons must meet some very stringent requirements such as high rated burst pressure with minimal wall thickness. The purpose of this thesis is to help reduce the amount of time invested in the experimental development stages of these medical balloons. This can be achieved with the aid of a cycle-to-cycle controller. The controller presented here may be simplistic, but it has shown that with further testing and modeling, it has the potential to completely replace the trial-and-error method of balloon development in use today.

Résumé

Le développement de nouveaux ballons d'angioplastie à partir de nouveaux matériaux peut être un processus très long et laborieux. Ces ballons doivent surpasser des normes rigoureuses tel qu'une pression d'éclat élevée avec une épaisseur de paroi minimale. L'objectif de cette thèse est de réduire le temps investi dans les étapes expérimentales du développement de ces ballons médicaux en utilisant un contrôleur cycle-à-cycle. Le contrôleur présenté dans ce document est simple mais il a néanmoins démontré qu'avec d'autres tests et un modèle amélioré, il remplacera éventuellement la méthode essais-et-erreurs présentement utilisée pour développer les ballons.

Acknowledgements

First and foremost, I would like to give my most profound gratitude to my supervisor, Dr. Benoit Boulet, for his help and guidance during this past year. Without him some of the work presented in this thesis would never have been possible. Although Dr. Boulet allowed me to work independently I always felt reassured that help was only a phone call away. I am indebted to him.

I would also like to thank the CNRC-NRC IMI for allowing me the use of their equipment to perform the experimental tests. Many IMI employees have welcomed me with open arms. Dr. Robert Di Raddo, your guidance, experience, and helpful suggestions on improving my thesis are very much appreciated. Christian De Grandpré and Marc-André Rainville, a big thank you is due to you both for always being there in the laboratory to answer my questions. You have made my stay at the IMI very enjoyable. I would also like to acknowledge Zoë Sarrat-Cave for her excellent work on angioplasty balloons, some which is used and referenced in this thesis. It was a pleasure working with you.

Thank you to my family. Words cannot express the gratitude I have towards my parents. You have both invested so much time, love, and money on me. You have always been very understanding and have supported me through thick and thin. I love you both. Last, but not least, a special shout should go to my big brother, Gino, for always being there for me. Thank you for being a great brother and guiding me in the right direction.

Table of Contents

List of Figures

List of Tables

List of Equations

Nomenclature

CNRC-NRC – Conseil National de Recherches Canada – National Research Council

IMI – Industrial Materials Institute

BFM – Balloon Forming Machine

DES – Double End Stretcher

ILC – Iterative Learning Control

TILC – Terminal Iterative Learning Control

PET – Polyethylene Terephthalate

PEEK – Polyetheretherketone

PVC – Polyvinyl Chloride

K_d – Derivative Controller Gain

K_i – Integral Controller Gain

K_p – Proportional Controller Gain

1 INTRODUCTION

A reduced amount of blood flow in the circulatory system may lead to serious health problems and possibly death. When the heart does not receive sufficient oxygen, severe consequences may result. Angina pectoris, for example, is a condition where pain is felt in the chest due to an inadequate amount of blood to the heart. Another worse condition is myocardial infarction, an illness where the heart tissue deteriorates due to the obstruction of the blood supply to the heart muscles. These illnesses are very common among elder people, and aside from cancer, they are two of the most frequent causes of death in the senior age group [1].

Millions of people throughout the world have circulatory problems due to arterial stenosis, a narrowing or blockage of an artery. Whether from genetic predisposition, or from lifestyle choices such as malnutrition and lack of exercise, this malady is increasing at an alarming rate. Until recently, arterial stenosis could only be corrected with bypass surgery. However since the early 1980's a more practical method called percutaneous transluminal coronary angioplasty, or PTCA, has for the most part, replaced bypass surgery. A PTCA balloon catheter is a medical device that is inserted into a clogged artery and inflated to a high pressure to clear the blockage. In simple terms, when the angioplasty balloon is inflated, it presses the calcified deposits into the vessel walls, creating an opening that improves blood flow. Unlike bypass surgery, the procedure is performed under local anesthetic and the patient's chest remains closed, reducing dramatically the recovery time [2]. Percutaneous transluminal coronary angioplasty has proven to be a much more efficient and safer method to reverse certain types of heart ailments such as angina pectoris and myocardial infarction.

1.1 Thesis Objective

The development and production of the ideal angioplasty balloon may take several months or even years. Companies who specialize in the manufacturing of these medical balloons still have not developed a straightforward method to produce them.

Unfortunately, balloons are still fabricated using *trial-and-error*, whereby tests are conducted by randomly varying inputs and the results evaluated. An unpredictable number of trials may be required, and thus, a more efficient method should be used to produce these balloons. This method involves modeling the balloon forming process and, from this, implementing a cycle-to-cycle (CTC) controller which will drastically reduce the number of trials needed to obtain the desired balloon.

Cycle-to-cycle controllers only adjust the input parameters once the cycle is complete as a goal to improve the next part. The *in-cycle* (IC) controller, on the other hand, is capable of adjusting the input parameters within the current cycle in the process to obtain the desired output. The clear advantage of the IC controller over the CTC controller is increased production rate and yield while reducing the scrap factor. A CTC controller might require several cycles before reaching the desired output, whereas a robust in-cycle controller could attain the same result within the first cycle of the process. However, in the development of angioplasty balloons, in-cycle control is not possible since, output parameters such as the balloon's burst pressure, wall thickness and compliancy can only be measured after the balloon is made.

The goal of this thesis is to study the effects of the micro-blow moulding parameters from the balloon forming machine on the outputs and propose a CTC controller which will reduce the production time of angioplasty balloons.

1.2 Benefits to the Industry

The design and eventual implementation of a CTC controller on the angioplasty balloon forming machine will be beneficial to the biomedical industry in many ways. Traditional balloon forming machines come with a touch screen software in which the user has to enter input values. Using trial-and-error, an operator must tweak the machine parameters after every cycle until the final blown part meets specifications such as no physical defects on the balloon, minimal wall thickness, and high rated burst pressure [1]. This procedure can be time-consuming and very costly.

The controller implemented is called *Iterative Learning Control* (ILC). Control theory such as ILC lets the users enter the desired outputs they wish to achieve. The machine then suggests the inputs that need to be entered that will most likely produce the desired outputs. Conformance to the required balloon characteristics is achieved much faster and with considerably less waste of angioplasty tubing. Hence, to summarize, the most notable benefits of ILC balloon development are as follows:

- Significant reduction of operator time.

- Clear increase in production yield.

- Reduced energy consumption.

1.3 Literature Review

There have been many advances in the design and manufacturing of medical balloons in recent years. More applications are found for these high-pressure balloons. Angioplasty, kyphoplasty, and drug-eluting balloons are but a few types common in the medical field today. This thesis, however, focuses exclusively on the angioplasty balloon and its fabrication process.

Over the past century medical device technology has made great strides in improving surgical procedures. Procedures, such as balloon catheterization, are now less invasive and require less recovery time for the patient. German physician doctor Werner Forssmann is credited as being the first person to perform human cardiac catheterization. He performed this operation on himself in 1929, at the young age of 25. Before attempting his own surgery, Dr. Forssmann approached his superior at a clinic in the town of Eberswald about inserting a catheter into his own heart. His superior denied permission deeming the procedure too dangerous. The young student then decided to attempt the experiment against his supervisor's wishes. Among the obstacles to overcome was access to the sterilization equipment, which could only be achieved with a nurse's consent. He convinced a nurse that the procedure could be done on her and it would be perfectly safe. Momentarily after the nurse brought him the instruments, he strapped her to the operating table and, instead of performing it on her; he did it to himself [8]. He anaesthetized his arm and "inserted a cannula into his own antecubital vein, through which he passed a catheter for 65 cm". He then "walked to the X-ray department, where he took a photograph of the catheter lying in his right auricle" [9].

In 1956, Dr. Werner Forssmann was awarded the Nobel Prize for his accomplishments and contributions to the medical field. A few years later, an American doctor, Charles Dotter, studied the dilation of narrowed arteries through the use of catheters. He opened narrowed leg arteries by gradually passing larger and larger catheters through them. However his work was not very popular in the United States. He decided to move to Europe where his work had a much warmer reception.

The following decade accelerated advancement in the field of medical device technology. In 1973, Dr. Porstmann designed a balloon catheter purposely for opening up the iliac artery, a major artery located at the top of the leg. Just a few years later, doctor Andreas Gruentzig, from the University Hospital of Zurich in Switzerland, performed the first documented balloon angioplasty surgery to open a blocked coronary artery. He spent many years designing the ideal balloon catheter which needed to be thin, flexible, and yet rigid enough to penetrate. He performed his first procedure in 1977, on a patient who suffered from angina pectoris. As a safety precaution, Dr. Gruentzig arranged for a team of doctors to stand by while he operated. If in the event there were complications, an emergency bypass could be immediately performed. However, the operation was a complete success and the patient had a quick recovery.

In 1980 Gruentzig immigrated to the United States where he could teach others his techniques. Andreas Gruentzig died tragically in a plane crash in 1985. His legacy, though, endured since, only a decade later, angioplasty surgery was being performed on over 200 000 thousand patients annually [8]. That number has steadily increased to an astonishing 2 million people worldwide per year in 2003.

1.3.1 Balloon Studies

There is little documentation covering angioplasty balloon technology. Two researchers, Dr. Michael Giese and Knut Sauerteig are well known for their pioneering work on angioplasty balloons. Dr. Giese is a mechanical engineer specializing in plastic and welding processes from the University of Erlangen. He is currently Division Manager for interventional cardiology at Biotronik in Berlin, Germany. Sauerteig is also a mechanical engineer with specialization in plastics at Biotronik. He is responsible for the development and application of extruded products such as heart catheters, guidewires, and stents used in PTCA surgery [2].

Sauerteig and Giese have published a number of articles in the Journal of Applied Medical Polymers over recent years. The article "The Effect of Extrusion and Blow Moulding Parameters on Angioplasty Balloon Production" describes the influence that the extrusion and blow moulding parameters have on the fabrication of angioplasty balloons [2]. We will limit our discussion to blow moulding parameters since extrusion is an entirely different technology.

The article covers the four main blow moulding parameters. They are the *primary temperature* or *warm-up* time, *forming temperature*, *applied pressure*, and finally the *stretch distance* of the tubing. The appropriate primary temperature is a function of the tubing material being used. When forming balloons, the two parameters that yield the best results are the low range of the material moulding temperature combined with a higher pressure. The resulting balloons are more consistent in quality, wall thickness and appearance [13]. Forming can be achieved at a higher temperature which will make the material softer and easier to shape. The applied pressure however must be reduced correspondingly as the temperature range increases. Interface Inc., a company that manufactures medical balloon forming machines, recommends a moulding temperature range of 54 to 71°C (327 to 344 K) for Pebax, a popular material for balloons.

Sauerteig and Giese believe that the applied pressure is the most influential input on the balloon's burst pressure index. Burst pressure is defined as the pressure at which the balloon will rupture. They claim that a balloon formed at 20 atmospheres of pressure (2

MPa) but at a lower temperature will have a higher rated burst pressure, approximately 2 atmospheres higher (202kPa), and a shorter required heating time than a similar balloon formed at 14 atmospheres (1.4 MPa).

The article concludes with a discussion on the importance of proper input selection in balloon manufacturing. Variation in one or two inputs can effectively change a balloon's wall thickness, burst pressure, and compliancy. Tests have shown that the resulting wall thickness is directly related to forming pressure, temperature and warm-up time. When, for example, the pressure is set high and the temperature low, the resulting balloon is typically thick-walled. These balloons characteristically have a higher rated burst pressure, but may not be the ideal choice because they are relatively difficult to fold and prepare for use in surgery. The measurement of wall thickness is the first step in the quality control process to determine whether a balloon will be accepted or rejected.

Other papers, such as the one presented at the 2004 ANTEC conference, include modeling polymer balloons used for angioplasty. This paper is the result of a collaboration between the Industrial Materials Institute, located in Boucherville, Québec, and McGill University. It focuses on balloon fabrication methods, the type of material used, and the range of balloon sizes possible. The three-dimensional finite elements model used simulates the balloon blow moulding process, the balloon folding properties, as well as its deployment within a clogged artery.

1.3.2 ILC Advancements

The first academic contribution to what today is commonly referred to as Iterative Learning Control is found in a technical paper written by Uchiyama in 1978. The paper was published only in Japanese, and unfortunately, it did not get the recognition that it deserved. It was only six years later, in 1984, that the ILC became a viable research tool, thanks in part to Japanese professor Arimoto. He published a paper in which he described a method that could iteratively validate model errors and disturbances [11]. In modern times, ILC theories are used in a myriad of applications in robotics, chemical processing, and mechatronic systems [12]. These applications utilize various forms of ILC theories including linear or nonlinear ILC, first-order or higher-order ILC, fixed or adaptive ILC, and finally continuous or discrete ILC. The following list shows to what extent the ILC theory has grown in popularity the last decade alone [12]:

- In 1993, Springer monograph had about 90 references on ILC.
- In 1993, ILC theory is taught during the summer session at Utah State University.
- In 1997, 30 out of 600 scientific papers were on ILC at the Asian Control Conference (ASCC).
- A learning control book is published by Jian- Xin Xu and Zeungnam Bien as a result of the 1997 ASCC.
- In 1998, a survey paper has approximately 250 ILC references.
- A searchable bibliographic online database, created by Yangquan Chen, has about 500 references on ILC.
- At least four Ph.D. dissertations on ILC have been recorded since 1998.
- Special sessions on ILC are offered at the 2000 ASCC and the 6th International Conference on Control, Automation, Robotics and Vision (ICARV).

This document will introduce the ILC theory to the development and manufacturing of angioplasty balloons. We believe the approaches described herein will bring significant advances in medical balloon forming technology. We are confident the proposed process improvements will significantly improve the production rate of balloons that are stronger and more consistent in quality.

2 BALLOON CHARACTERISTICS

Modern day medical balloons are made in a wide range of shapes and sizes. There are also complex custom shapes for specific applications. Angioplasty balloons may vary from 1 to 25 millimeters in diameter, with single wall thickness ranging from 0.015 to 0.025 mm. Larger and thicker balloons are usually used to open up coronary arteries, whereas thinner ones are used for minor arteries. One amazing characteristic about these medical balloons is their ability to withstand relatively high pressures. With a single-wall thickness approximately one-tenth that of a strand of hair, some balloons can handle up to 30 atmospheres of pressure, or about 3 MPa without rupturing.

2.1 Balloon Description

Angioplasty balloons are composed of five descriptive areas (see figure 2-1). The extreme ends of the balloon are called the necks and they are usually different in size. The *proximal neck* is the side of the balloon with the larger diameter, whereas the end with the smaller diameter is the *distal neck*. The smooth cylindrical part of the balloon is called the *body*. The diameter and length of the body are the defining parameters of the balloon. As an example, a balloon with a body 3 mm in diameter and 15 mm in length is said to be a 3 x 15 mm balloon.

Finally, the conical parts of the balloon are called the cones. The *proximal cone* connects the proximal neck to the body and the *distal cone* connects the distal neck to the body. These parts are usually much thicker than the body since they are expanded less. A typical balloon cut is shown in Figure 2-1 on the following page.

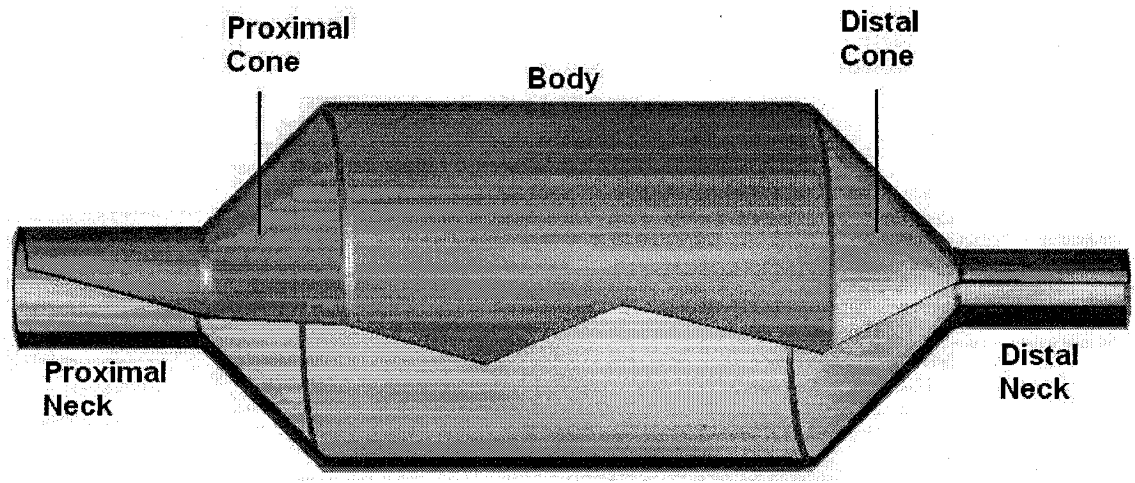


Figure 2-1 Descriptive areas of a typical angioplasty balloon

When a balloon bursts, it usually splits along its length rather than radially. This is because the radial stress is typically twice as strong as the axial stress on the balloon surface. The relationship between the two is derived. The variables are pressure, diameter and thickness [3]:

$$\sigma_r = 2\sigma_a$$

$$\text{Radial Stress } \sigma_r = \frac{pd}{2t}; \quad \text{Axial Stress } \sigma_a = \frac{pd}{4t}$$

Equation 2-1 Stress Equations

This is desirable, because if an angioplasty balloon were to burst inside a patient during a surgical procedure, it can be retrieved with relative ease without causing any complications. However, if the balloon were to tear in the circumferential direction during the medical procedure, it would be significantly more dangerous since the front portion of the balloon could remain stuck in the patient's artery during its removal.

2.2 Medical Applications

Like almost all other technologies, angioplasty balloon technology expanded exponentially since the seventies and eighties when balloons were first introduced into the medical field. Modern high-pressure balloons are thinner, much stronger and have smaller profiles. They can be applied to a wide range of minimally invasive procedures. Kyphoplasty balloons, for example, are minimally invasive medical balloons used to treat fractures caused by osteoporosis. This procedure helps stop the pain caused by the bone fracture and restores the vertebral height lost due to the compressed fracture [6]. The pictures in Figure 2-2 depict the major steps applied in the procedure [15].

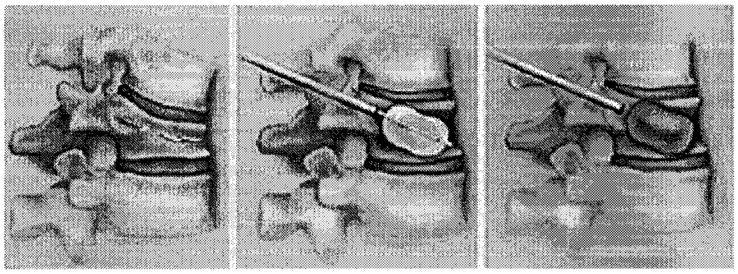


Figure 2-2 Kyphoplasty balloon procedure (Permission to print granted by Dr. Gerszten from the Department of Neurological Surgery at the University of Pittsburgh Medical Center)

Kyphoplasty is usually done under general anesthesia. Similar to angioplasty surgery, a balloon catheter is guided into the vertebra and inflated with a liquid. As the balloon inflates, it restores the collapsed vertebra to its original position. Once inflated to the nominal size and the vertebral column is properly aligned, the balloon is deflated and removed, creating a cavity. This cavity is then filled up with bone cement which later hardens and maintains the corrected vertebra [16].

The improved reliability of angioplasty balloons made it possible for doctors and engineers to design new more aggressive affiliated medical devices. As a result, there is virtually no limit to the diagnostic and therapeutic procedures to which high-pressure balloon technology can be applied to dilate blockages in the body. Some of the more common applications are as follows [7]:

- Tear duct dilatation
- Carpal tunnel dilatation
- Esophageal dilatation
- Billiary dilatation
- Urethral dilatation
- Fallopian tube dilatation
- Heart valve dilatation (i.e. valvuloplasty)

The variety of high-pressure balloons used in 21st century minimally invasive surgery is enormous. Balloons are selected depending on the type and location of the ailment that needs to be treated. Each balloon is chosen with the neck, cone, and body shapes to enhance the task at hand such as opening an artery, delivering a drug or displacing tissue.

2.3 *Types of Medical Balloons*

2.3.1 High-Pressure

Medical balloons can be broken into two basic classes. The first is the high-pressure, non-elastic balloon used to apply force in a given area. Angioplasty balloons fall into this class. High-pressure balloons are fabricated from non-compliant materials. Balloon compliance is the term used to describe the degree to which a balloon's diameter changes as a function of pressure. In other words, it is the degree, or the extent that a balloon can expand from its original shape. A balloon that expands to two or three times its original size is more compliant than one that barely changes. The most fundamental characteristic of angioplasty balloons is their ability to withstand significantly high pressures with very little stretching of the balloon walls. When inflated at the nominal rated pressure (i.e. the pressure applied into the balloon during surgery), non-compliant balloons might only expand 110 percent of their normal size. A predictable pressure/volume relationship is a must when performing arterial dilatation surgery since too much volumetric increase might lead to rupture of the arterial wall [3].

2.3.2 Low-Pressure

Low-pressure balloons are generally elastomeric in nature and are made of resilient materials such as latex and silicon. Unlike high-pressure balloons, these balloons usually return back to their original shape and size once the pressure is reduced. Low-pressure balloons are considered very compliant since they are able to expand to several times their original size. Thus these balloons cannot reliably maintain dimensions when inflated or retain well defined shapes at higher pressures [3].

2.4 Balloon Materials

Angioplasty balloons were first created using flexible polyvinyl chloride (PVC) plastic. They weren't as practical as modern day balloons due to their relatively thick walls and low burst pressure results. During the early eighties, crosslinked polyethylene and polyester polyethylene terephthalate (PET) eventually replaced the PVC resin. Nylon balloons came out in the late 80's, and polyurethane balloons followed in the early 90's. Today, most high-pressure medical balloons are made either from PET, Pebax®, or nylon. PET offers advantages in tensile strength and maximum pressure rating while nylon is softer and can fold more easily [3].

2.5 Balloon Formation Process

The first step in the balloon production process is to extrude the tubing. At the moment, the tubing used to make angioplasty balloons at the Canadian National Research Council (CNRC-NRC IMI) in Boucherville is purchased from plastic extruding companies. However, once more research and testing are completed, the CNRC-NRC IMI plans to extrude its own tubing for medical balloons.

2.5.1 Tube Extrusion

The balloons described in this thesis are developed from a polymer compound called Pebax®. It is produced by the Technical Polymers Group of ATOFINA Chemicals Inc. Pebax® has a high rated burst pressure combined with an average compliance. Because these balloons can withstand much higher pressure than the nominal pressure needed to dilate a diseased artery during surgery, the low risk of rupture makes the product relatively safe.

The choice of the proper material and the identification of the appropriate extrusion characteristics can be a tricky process. The CNRC-NRC IMI focused its research on two sizes of Pebax® tubing to make angioplasty balloons. Tubing used to make 3 x 15 mm balloons comes from Innovative Extrusions in California. The larger tubing used to blow 8 x 30 mm balloons is extruded by Extrusioneering, also located in California. A table with the tubing specifications is shown below.

	Tubing for 3mm Balloon	Tubing for 8mm Balloon
COMPANY	Innovative Extrusions	Extrusioneering
MATERIAL	Pebax®	Pebax®
DUROMETER	72D	72D
DIMENSIONS	0.036" x 0.0195" x 6'	0.088" x 0.058" x 6'
QUANTITY	1000 ft	1000 ft
LOT NUMBER	FP031904-001	030424-3-C
PURCHASE ORDER	10396	0007905

Table 2-1 Tubing Specifications

The durometer index value is an indication of material hardness. A material index value of 'A' is generally a softer material while those with an index value 'D' are harder.

2.5.2 Tubing Verification

Extruded tube quality is the crucial element in the manufacturing of high quality angioplasty balloons. Each section of tubing must be meticulously examined before inserting it in the balloon forming machine. Quite often tubing defects such as "fish eyes" or air bubbles occur during the extrusion process. This happens when air gets trapped in the material during tube formation.

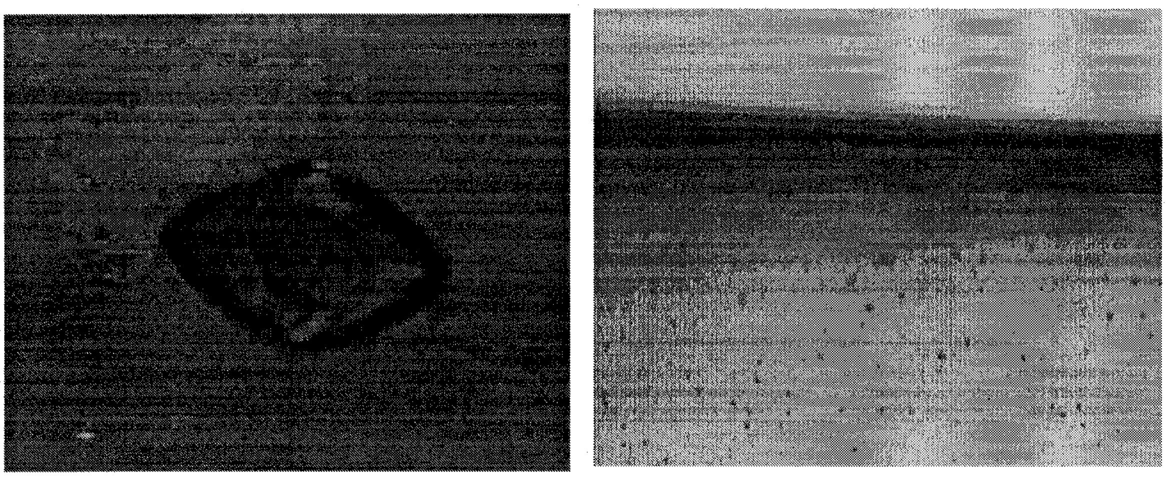


Figure 2-3 Example of (a) fish eye and (b) scratches

It is also quite common to find scratches. Extruded tubes with surface scratches will more likely produce inferior quality balloons. Tubing processed with such defects must not be used and should be discarded. An example of these defects may be found in the figure above.

Polymer tubing that is acceptable moves on to the double-end stretcher machine. Basically, this machine prepares the tubing so that it fits into the balloon forming machine where a balloon will be formed via micro-blow moulding. Once blown, balloons are visually inspected for defects and subjected to a number of validation tests. Acceptable balloons are then packaged and prepared for surgery during the catheter assembly phase. A schematic of this procedure, provided by Zoe Sarrat-Cave, an intern in the biomedical lab at CNRC-NRC IMI, is shown in Figure 2-4.

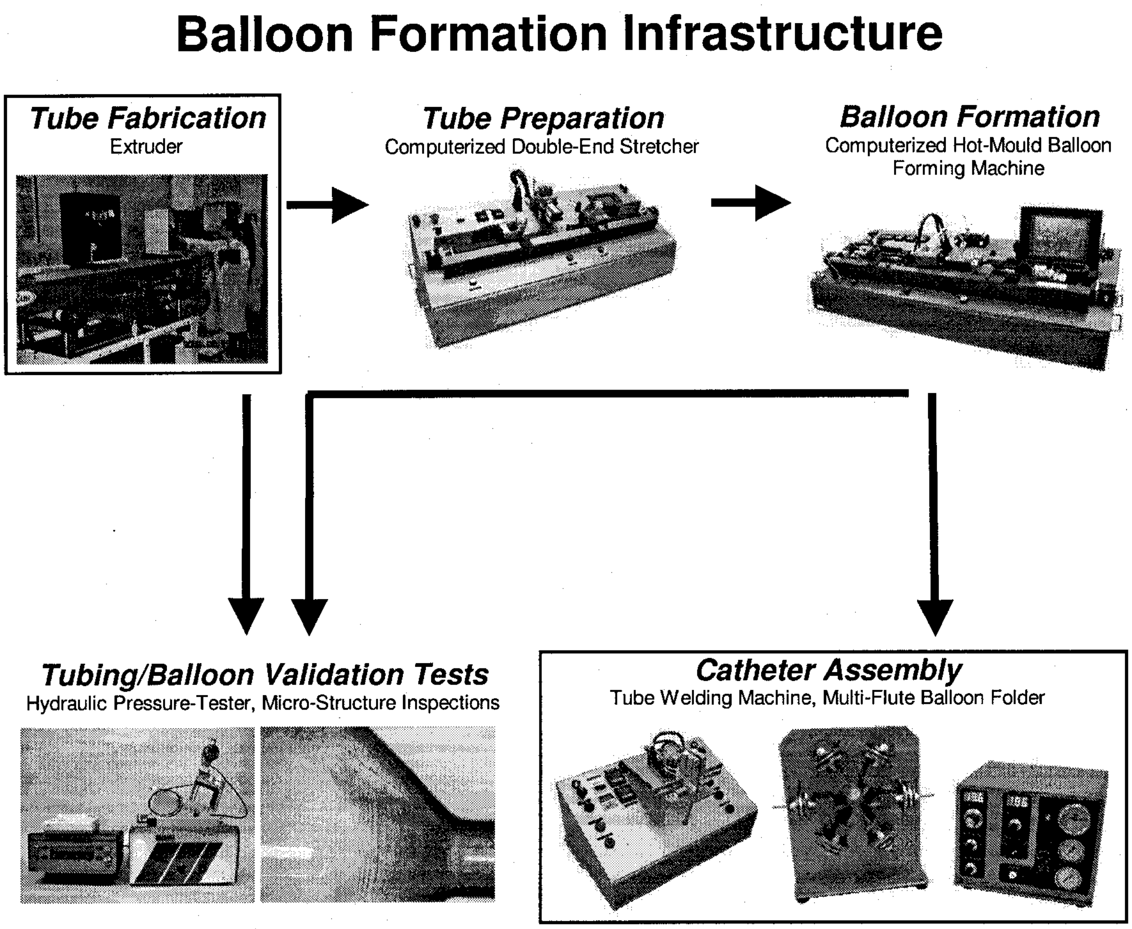


Figure 2-4 Balloon Fabrication Infrastructure (Permission to print granted by Interface Associates)

3 BALLOON FORMING EQUIPMENT

There are two machines involved in the fabrication process of angioplasty balloons. The first, called Double-End Stretcher, prepares tubing for the Balloon Forming Machine. In this chapter, the reader will gain a better understanding of how both balloon forming equipment function and how to operate them.

3.1 The Double-End Stretcher

Generally tubing used to form balloons needs to be necked down in order to fit through the end plugs of the Balloon Forming Machine (BFM). This is achieved with the help of the Double-End Stretcher (DES). The DES basically stretches both sides of a tube while leaving an unstretched length in the middle. This unstretched section, called parison, is the part of the tubing that will be blown up into an angioplasty balloon.

Even when the tubing does fit through the end plugs of the BFM, it is still suggested by Interface Associates Inc., a leading manufacturer of balloon forming equipment, to form a parison because it provides improved consistency when blowing balloons. The parison length determines how much material is available to expand the balloon. Shorter parisons tend to form balloons with thinner walls whereas longer parisons lead to thick-walled balloons. A good parison length to start developing balloons is ⅔ to ¾ of the desired balloon length, according to Interface Associtеs Inc. Thus, to form a 3 x 15 mm angioplasty balloon, a parison length of ten to twelve millimeters would be adequate. A typical DES machine, obtained from the Interface Associates Inc. website, is shown in Figure 3-1 [17].

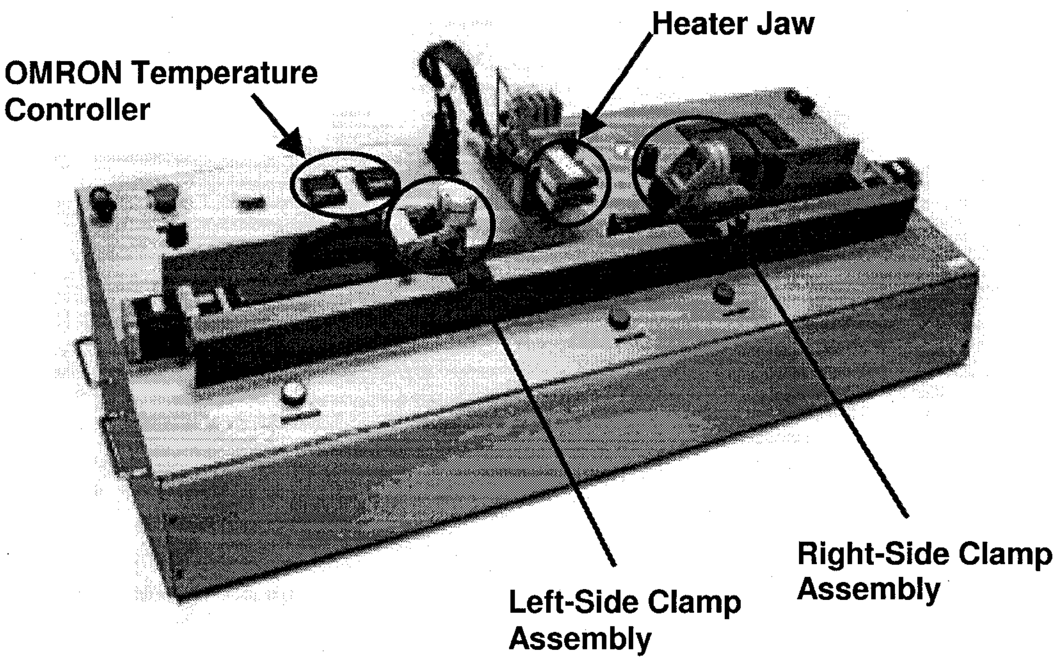


Figure 3-1 Double-End Stretcher (Permission to print granted by Interface Associates)

3.1.1 DES Components

There are three main components to the Double-End Stretcher. The heating cartridge, or heating plates, basically heats the section of tubing which needs to be stretched. Shown above is a machine featuring an OMRON temperature controller that lets the operator keep track of and adjust heating temperature. A jaw temperature of 150C for Pebax® is the norm. The heating time on each side varies depending on tubing size. Smaller tubing typically takes five to ten seconds whereas larger tubing may require twenty to forty seconds. Integral cooling ducts promote rapid cooling of the tubing after stretching and avoid any possibility of recoil. This step is critical since uncooled tubing released immediately after stretching would likely form a "pig tail" and would have to be discarded. An additional benefit of rapid cooling is the re-strengthening of the material. The final components of the DES are clamp assemblies that simply hold the tubing in place during stretching. Figure 3-2 provides a closer view of these parts.

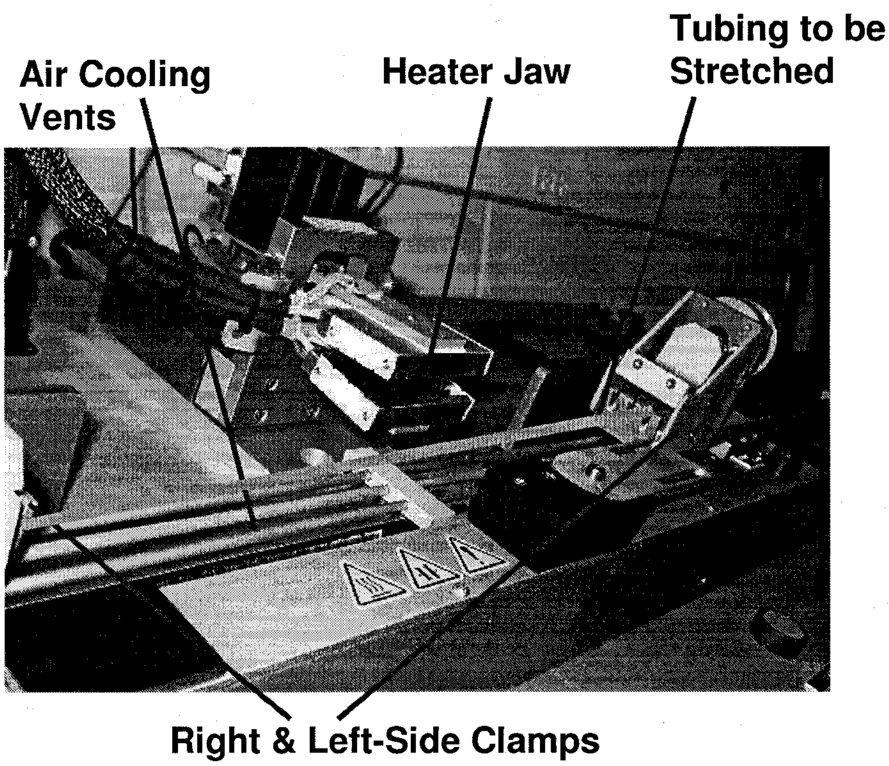


Figure 3-2 DES Components (Permission to print granted by Interface Associates)

3.1.2 DES Procedure

The Double-End Stretcher operational procedure is quite straightforward. The first step is to insert the tube into the machine and clamp both ends. Then, one side is heated for a certain length of time, depending on the input entered, and stretched out a certain distance. Finally, the cooling ducts are activated and the tubing is cooled back down to room temperature. The identical process is repeated for the other side. The following picture compares the shape of two typical parison sizes. The larger tube is used to blow 8 x 30 mm angioplasty balloons while the smaller one is used to blow 3 x 15 mm balloons.

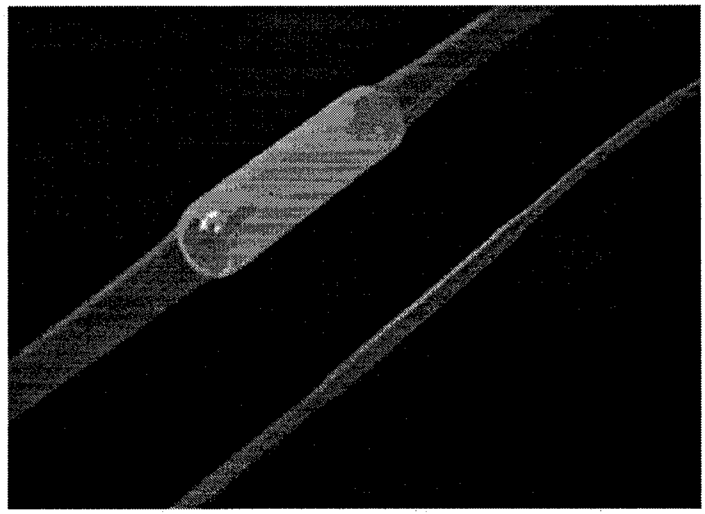


Figure 3-3 Parison to form (a) 8 x 30 mm balloon and (b) 3 x 15 mm balloon

The following diagram, provided by Zoe Sarrat-Cave, illustrates the parison forming sequence pictorially.

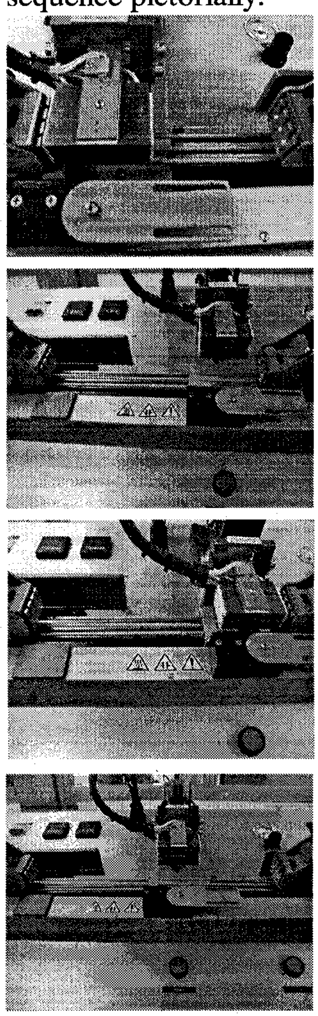
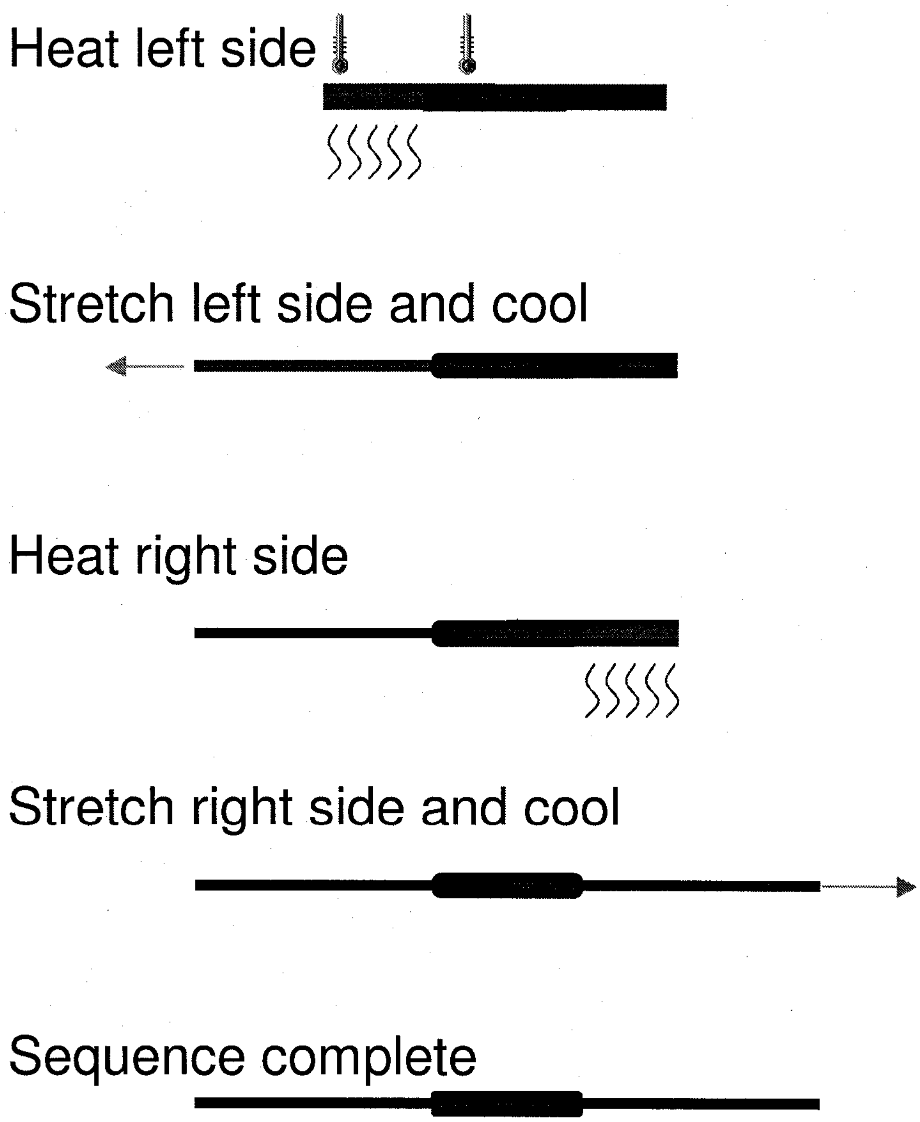


Figure 3-4 DES Procedure



Refer to Appendix A for a more complete overview of the DES operating procedure.

The photograph below shows the DES machine while forming parisons on three tubes simultaneously. When stretching only one or two tubes any of the three clamp positions is acceptable. Tests have shown that the parison is practically identical in anyone of the three clamp positions.

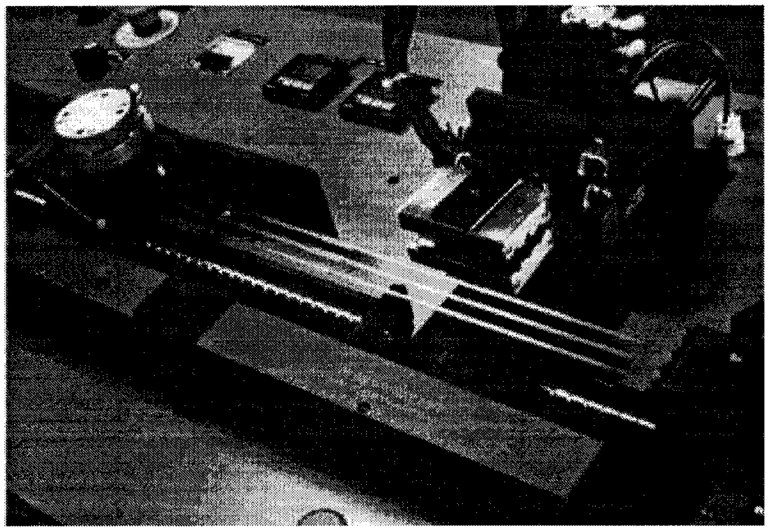


Figure 3-5 DES forming three parisons simultaneously (Permission granted by Interface Associates)

3.1.3 DES Inputs

The DES is equipped with a touch screen user interface which allows the operator to enter various inputs. The inputs for both the left and right sides are as follows:

1- Stretch speed in mm/s
2- Stretch distance in mm
3- Heat time in seconds
4- Cool time in seconds
5- Desired unstretched length in mm

A picture of the touch screen is shown in Figure 3-6.

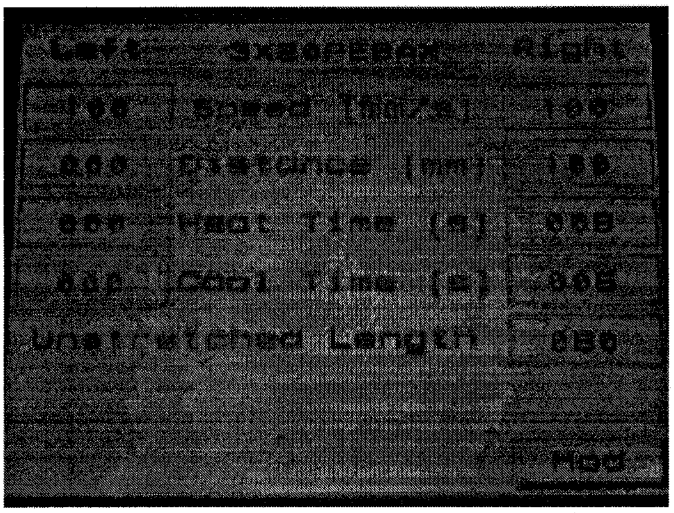


Figure 3-6 DES Input touch screen (Permission to print granted by Interface Associates)

3.2 Balloon Forming Machine

Most medical balloons, including angioplasty balloons, are formed via blow molding. More specifically, it is considered as a micro-blow molding technology. The heating process runs in a discontinuous cyclic manner [2]. In other words, each cycle is only capable of producing one balloon. When the cycle ends, the Balloon Forming Machine has to be reset before forming another.

Initially an extruded tube is inserted into a beryllium copper mold. One end of the tube is clamped while the other end is clamped and connected to a compressed air supply. The input parameters are set, and the forming cycle begins. A Picture, from the Interface Associates Inc. website, of the Balloon Forming Machine is shown in Figure 3-7 [17].

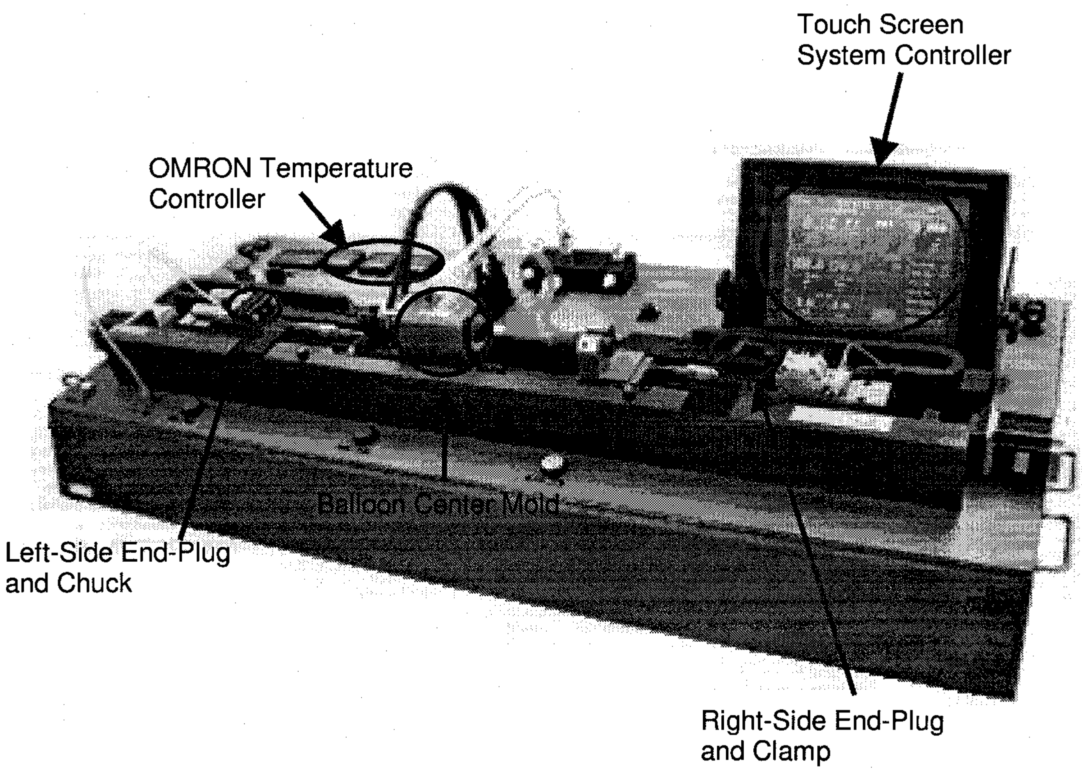


Figure 3-7 Balloon Forming Machine (Permission to print granted by Interface Associates)

3.2.1 BFM Components

The Balloon Forming Machine operates with a mold and two end plugs made from a beryllium copper alloy. It is in the cavity within these parts that the balloon is formed. One end of the mold has a clamp with an air supply. The other end is equipped with only a clamp to ensure that the tube is well secured. Also integral with the mold assembly are the heater and water jacket. The heater heats the tubing before blowing pressure is applied. The water jacket cools the mold back down to room temperature once the blow-molding pressure is released. A close-up of these components can be seen in Figure 3-8.

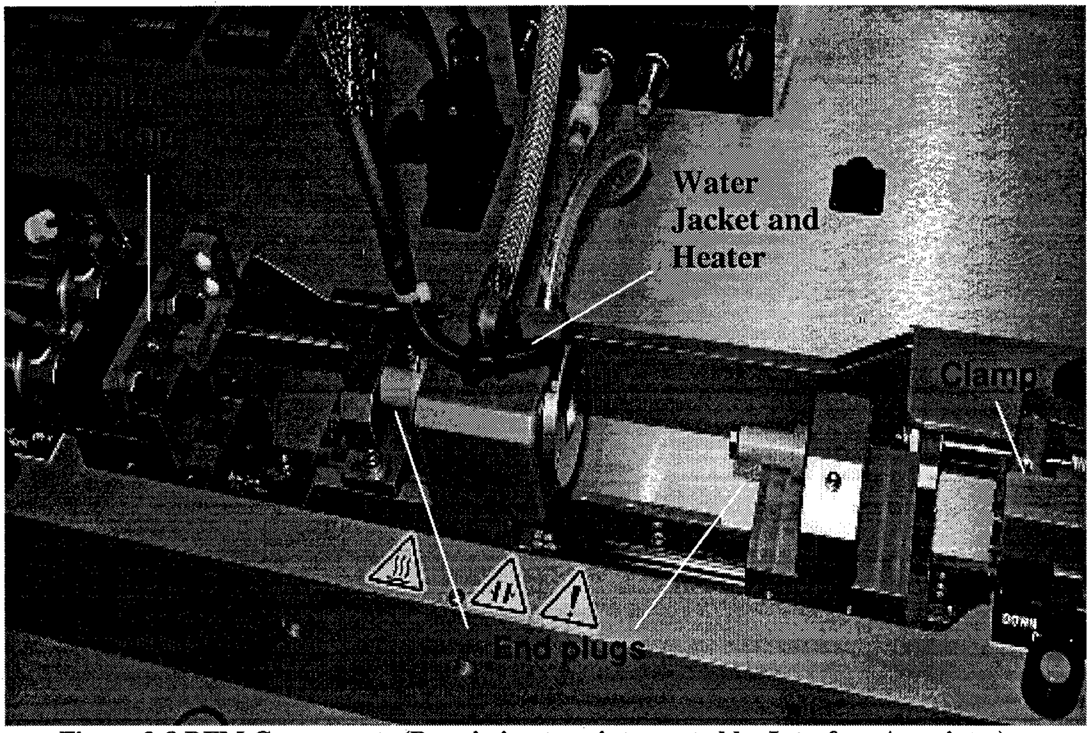


Figure 3-8 BFM Components (Permission to print granted by Interface Associates)

3.2.2 Mold and End Plugs

The base material for the center mold and end plugs offers several advantages. Beryllium copper alloy (98% Cu and 2% Be) has excellent heat and electrical conductivity, superior strength, and is relatively resistant to oxidation [4]. The grayish plastic material in the end plugs (see Figure 3-9) is polyetheretherketone, more commonly known as peek. Peek is a semi-crystalline thermoplastic which can withstand temperatures well above 260 °C, a level often necessary when forming angioplasty balloons. A characteristic of Peek is that it may be reinforced with graphite fibers; a material used in these end-plugs [5]. The graphite is used to isolate the part of the tubing which is not required to be heated. Although the graphite material is not seen in the picture below, it is shown in the following section.

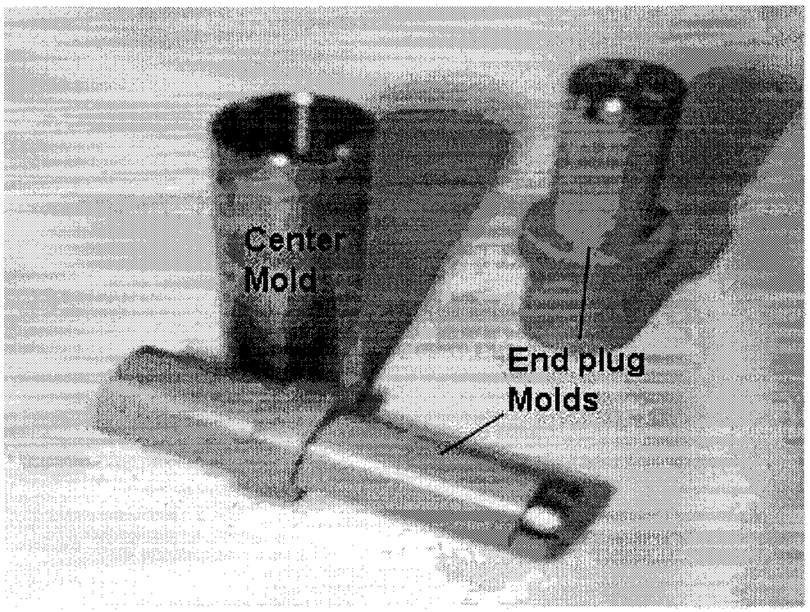


Figure 3-9 Center Mold and End Plugs (Permission to print granted by Interface Associates)

3.2.3 Design of Mold and End Plugs

Interface Associates Inc. generously provided dimensional data through AutoCad files. However, since this program shows the parts only in two-dimensions, the author used the dimensional data to develop a solid three dimensional model using solid modeling software. Figure 3-10 is a design of a typical mold used to form angioplasty balloons along with a cross-sectional view.

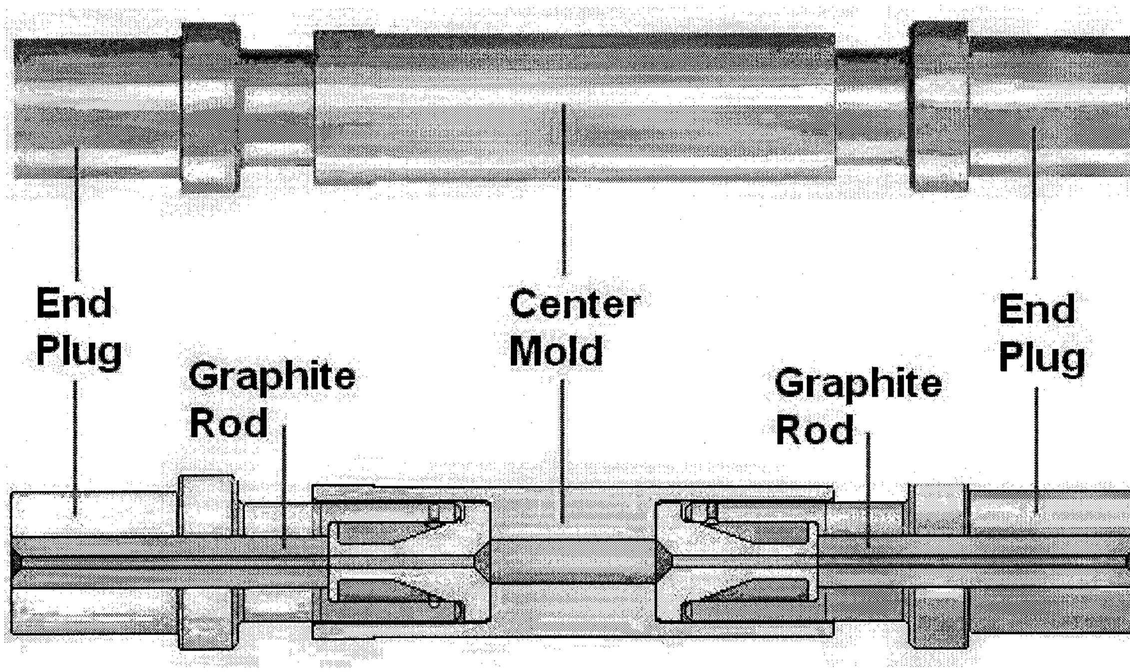


Figure 3-10 Design of Center Mold and End Plugs

3.2.4 Micro Blow-Molding Process

The tubing is heated in the mold at a low constant pressure for a defined length of time. This stage is called the warm-up period. When the warm-up time has elapsed, whether defined as a specific number of seconds or by the attainment of the required temperature, the system automatically increases the forming pressure for a specified length of time. This phase is the forming time. Several seconds after switching to the forming pressure, an axial stretching, or primary stretch, begins at both ends of the already expanded tubing. The figure 3-11 gives an indication of the progression as the angioplasty balloon is expanded inside the cavity.

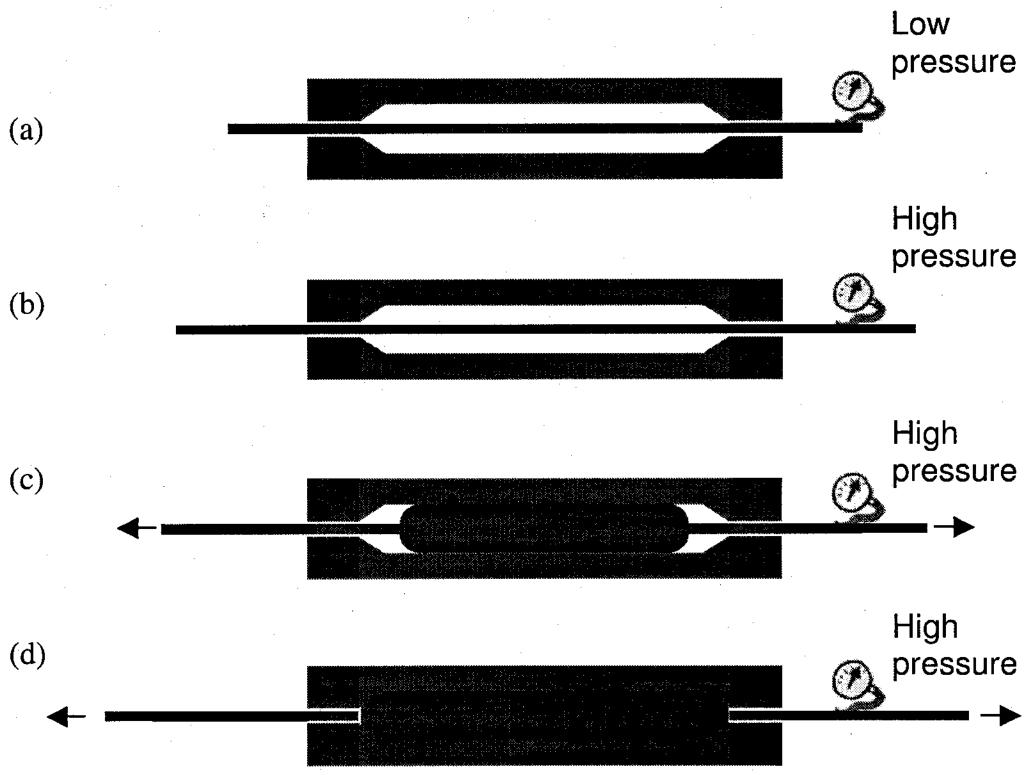


Figure 3-11 (a) Primary Heat (b) Primary Stretch (c) Balloon Formation (d) Secondary Stretch

Next, the mold temperature is increased again and a secondary stretch is done to define the cones at both the proximal and distal sides. The secondary stretch thins out the balloon neck to get the desired inner diameter. Longer secondary stretches will open the IDs more and lead to thinner wall thicknesses in the cones. The increase in temperature before applying the secondary stretch helps soften the material so that it does not rip in the middle during additional stretching. Finally, cooling takes place after forming, by circulating water in the mold, and then finally purging it.

To help the operator better understand and visualize this micro-blow molding process, Figure 3-12 [17], with the input parameters is shown below. In this example, the balloon is initially heated to 200°F (366 K). Once this temperature is attained, a high pressure of 425 psi (2.93MPa) is applied with a primary stretch of 70 mm. The application of pressure to the heated tubing forces radial expansion that fills the mold cavity to form a balloon. Next step is to define the cones. After 7 seconds the mold temperature is again increased to 285° F (413K) and a secondary stretch is set to 113 mm. At this stage the angioplasty balloon is blown to its final shape. Finally, the pressure is reduced and the mold is cooled to its original temperature. The mold is then opened and the balloon is ready to be retrieved.

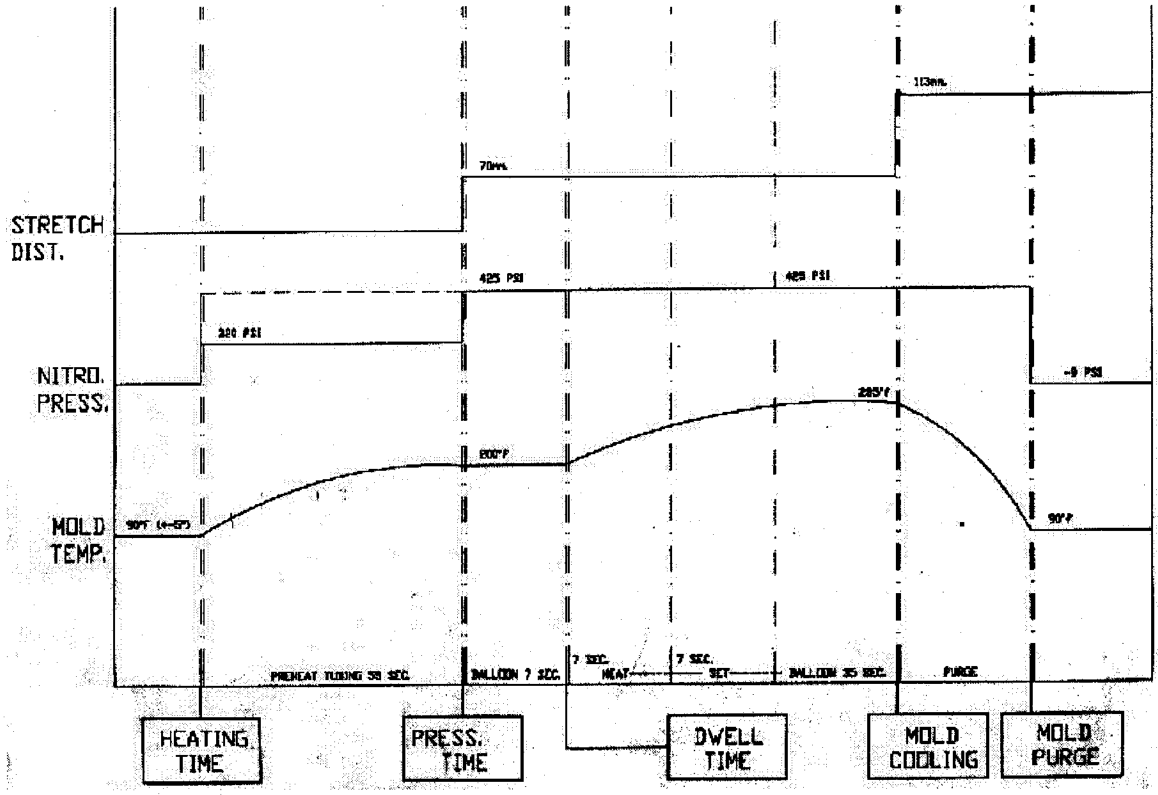


Figure 3-12 Blow molding process (Permission to print granted by Interface Associates)

3.2.5 BFM Inputs

The Balloon Forming Machine is very user friendly given that it can be operated by either touch screen or by computer. The touch screen version is shown in Figure 3-13.

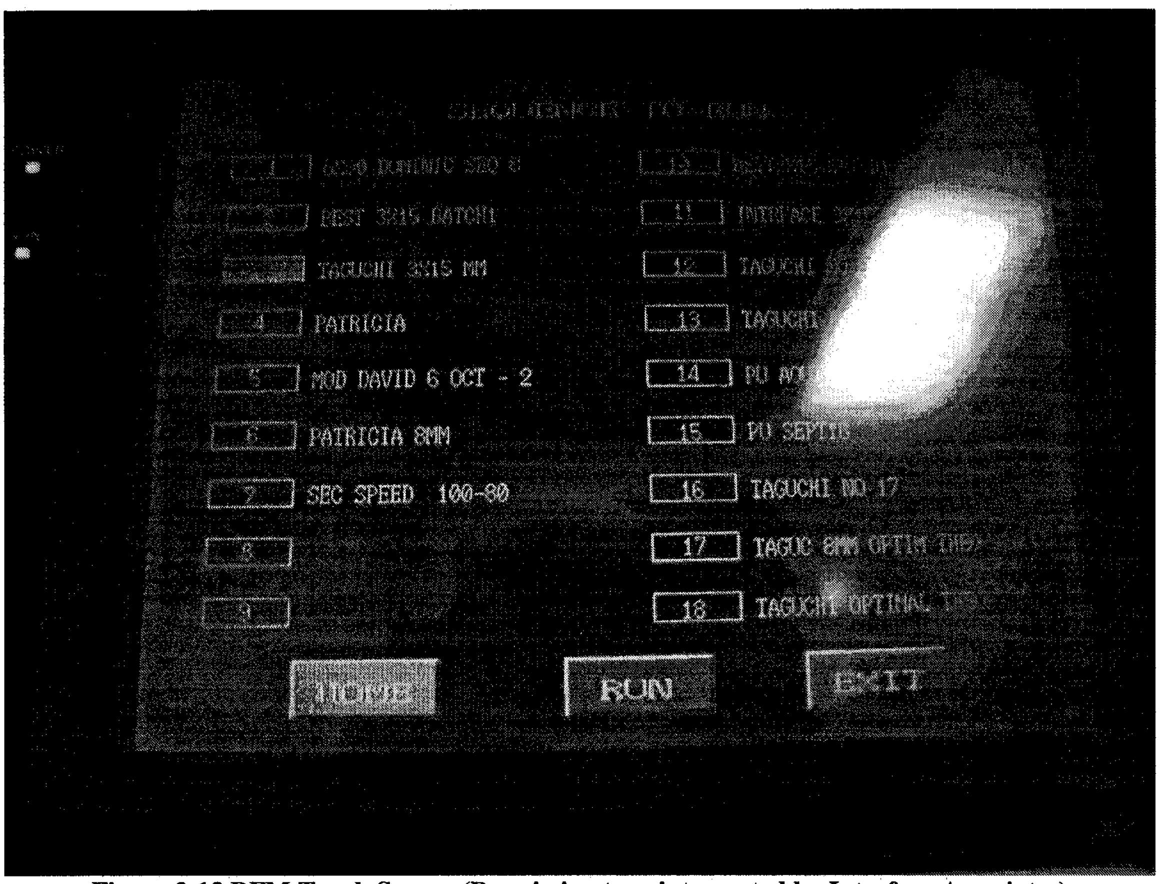


Figure 3-13 BFM Touch Screen (Permission to print granted by Interface Associates)

A port is located on the backside of the machine where information from the computer can be downloaded to the BFM. When several changes must be made at one time, it is easier to make them from the computer rather than directly on the machine. Similarly, if a review of all the inputs for every blow molding step is desirable, information from the BFM can be easily uploaded to the computer. A typical overview screen is shown on the following page.

	STEPS ->		01	02	03	04	05	06	07	08	09	10	11	12
SET VALUES	Heat (C)	Left												
		Center				90	90	90	141	134				
		Right												
	Cool (on/off)	Center									X			
		Plugs									X			
	Purge (on/off)	Center										X		
		Plugs										X		
	Pressure (Bar)	Set To				35						0		
		Fill Rate				10						31		
		Dump										X	X	
		Vacuum												
	Stretch (mm)	Left		15	0	1		12		16				60
		Right		0	0	1		12		16				100
	Speed (mm/s)	Left		80	80	20		130		100				40
		Right		80	80	20		130		100				60
	Force (N)	Left		53.4	53.4	53.4		53.4		100				5
		Right		53.4	53.4	53.4		53.4		100				5
	Clamps Down	Left			X									
		Right			X									
	Mold Closed			X	X	X	X	X	X	X	X	X	X	
STEP EXIT	Heat (C)	Left												
		Center				>80			>120	>130	<35			
		Right												
	Force (N)	Left												
		Right												
	Pressure (Bar)												<2.5	
	Position (mm)	Left												
		Right												
	Time (s)						0.2	2				7		10

Figure 3-14 BFM Input overview (Permission to print granted by Interface Associates)

A quick walk through the chart reveals the typical inputs entered into the Balloon Forming Machine. No data is entered in the column of step one. The BFM starts functioning at step two where the stretch, speed, and force inputs are entered with the mold closed. The left clamp is still open at this point and is moved 15 millimetres to the left of the *home* position. The home position is located at the middle of the machine. The shifting of the left clamp allows the operator to work with more room when clamping the tubing. Once the tube is properly inserted, the left clamp shifts back to the right by 15 millimetres. The 'X' for *clamps down* left/right informs the user that the clamps are activated and the tubing is locked in place.

In step four the blow molding process begins. First, the tubing is stretched from each side by 1 millimetre at a speed of 20 mm/second and a force of 53.4 Newton to ensure that it remains tense and does not sag. The central part of the mold is heated to 90°C (363K) and a pressure of 35 atmospheres (3.55 MPa) is applied, as previously noted, from the left clamp, with a *fill rate* of 10. The fill rate is the degree of the opening of the needle orifice where pressure is released. Fill rate may vary from 1 to 31 with 1 being the smallest opening and 31 the largest. In this chart, once the mold attains a temperature greater than 80 °C (353 K), the input sequence moves to the next step. Step five involves no changes except for a time exit condition of 0.2 seconds. This minimal time allows the BFM to collect all necessary information such as the mold temperature that needs to be downloaded to the computer and later analyzed. In step six, a *primary* stretch of 12 millimetres on each side at a speed of 130 mm/second is applied. When the pressure within the tubing is greater than the resistance strength of tubing walls, expansion begins until the balloon fills the mold cavity. This entire step only takes a fraction of a second to complete. Therefore, to be on the safe side, a step exit of 2 seconds is entered before moving on. Greater stretches result in balloons with thinner walls and thinner necks.

Following the primary stretch is the *secondary* stretch used to define a balloon's cones. This step is also intended for defining the inner diameters of the proximal and distal necks when assembling an angioplasty balloon to a balloon catheter. As previously mentioned, a secondary stretch requires an increase in mold temperature to avoid tearing. In this example, at a temperature of 121 °C (250 K), an additional pull of four millimetres on each side is applied for a total stretch of 16 mm.

At this point the balloon is completely formed and cooling begins. The water jacket circulates cold water from the water basin into the mold and end plugs. This procedure usually takes a couple of minutes depending on the mold temperature. In this chart, once the mold attains a temperature below 35 °C (308 K), the BFM begins to purge the water from the mold and end plugs and dumps it back into the water basin. Pressure is then released from the mold. Next, the clamps release the tubing and move away to help facilitate balloon retrieval from the center mold. The angioplasty balloon is then ready for observation and testing.

A step-by-step protocol used to form angioplasty balloons at CNRC-NRC IMI is included in Appendix B. The illustrations and explanations in this section were graciously provided by Zoe Sarrat-Cave.

4 BALLOON ASSEMBLY

Once an angioplasty balloon is completed and tested it is then assembled to a guiding catheter used for heart surgery. The catheter is the other major part of the balloon angioplasty system. The guiding catheter plays a very important role in angioplasty balloon surgery. Without a functional catheter able to navigate the narrow and tortuous passageways within a diseased artery, it would not be possible for an angioplasty balloon to reach its destination and clear blockage [24].

This chapter helps better understand how a verified angioplasty balloon is welded to a balloon catheter for use in PTCA surgery. The author acknowledges Annie Poirier, a summer intern at CNRC-NRC IMI, for her excellent work on the study of balloon assembly. The majority of the information in this section is the result of her work during summer of 2004.

4.1 Catheter Thickness

Catheters are required by design to be as thin and non-invasive as possible. However, there is a limit to catheter minimum thickness. The guiding catheter must be big enough to contain the balloon catheter. Other factors affect the thickness of the catheter as well. The catheter wall thickness needs to be sufficient to support the pressures applied to inflate the balloon. In all cases the burst pressure of the catheter must be higher than that of the balloon. Thin catheters may be high on maneuverability but might be low on axial rigidity. Overly thin catheters are likely to buckle and coil as they are nudged forward inside the blood vessels. Thicker, more rigid catheters are stronger but less flexible. If the catheter is too stiff, it can damage vessel walls as it is guided along the contour of the vessel system. Such damage may provoke an injury response that can lead to restenosis and possible occlusion of the vessel [25].

A balloon catheter is shown in Figure 4-1 [19].

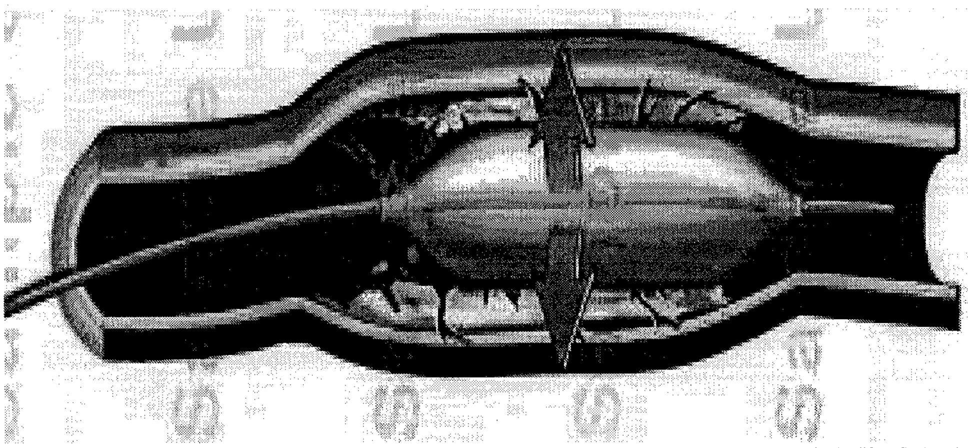


Figure 4-1 Balloon Catheter (Permission to print granted by Nucleus Medical Art)

4.2 Welding Order

Angioplasty balloons with superior performance characteristics and free of physical defects are subsequently mounted on a catheter. A balloon is usually welded on the catheter as follows:

Step 1- Welding of the distal axe (proximal side of the balloon)
Step 2- Welding of the internal catheter (distal side of the balloon)
Step 3- Welding of the exit port (Rapid-exchange platform only)

Steps two and three may be reversed if desired.

Acceptable balloon assemblies will have tightly welded invisible joints. But most importantly, they will invariably have burst pressure ratings higher than that of the angioplasty balloon.

4.3 Components of the Welded Assembly

The selection of the proper welding material is critical when welding the balloon to the catheter. In order to make a perfect weld, it is imperative to have in hand:

i) The medical balloon which will be mounted onto the catheter. Once the fabricator has found the best possible balloon, exact measurements of the inner and outer diameters of the proximal and distal sides of the balloon are required. Having chosen the proper balloon dimensions will help predict the size of the welding jaws.

ii) The welding jaws and the thermal screen. More specifically, an exact diameter of the groves in the thermal screen shown below is needed.

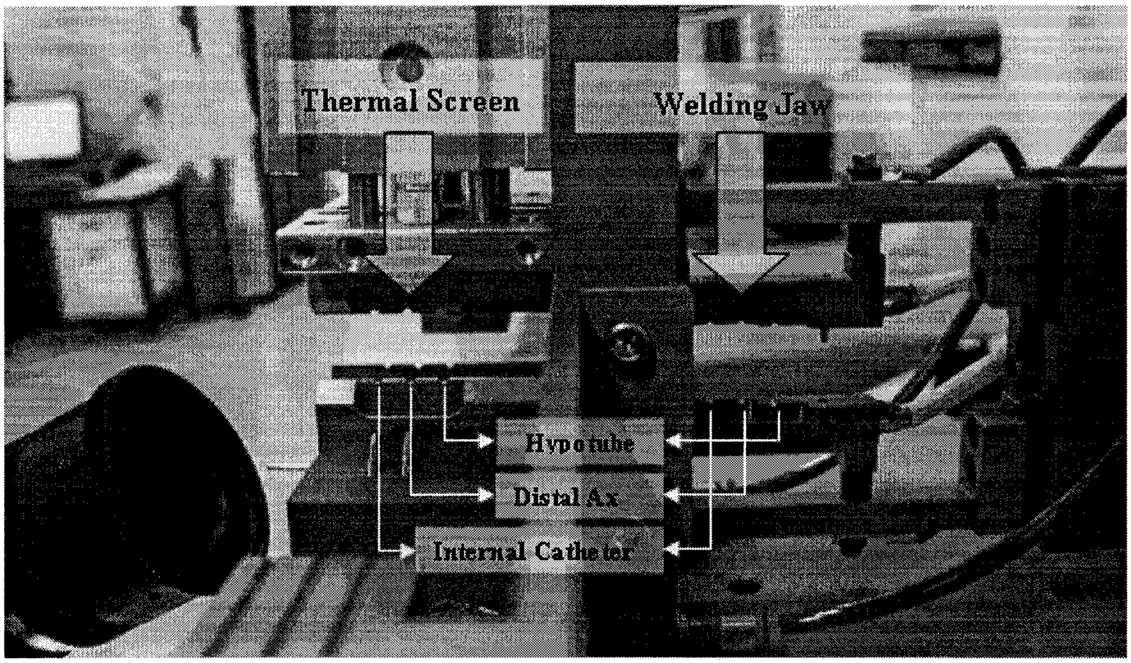


Figure 4-2 Welding Machine Parts (Permission to print granted by Interface Associates)

4.3.1 Assembly Platform Options

The type of assembly platform depends on the balloon's function. There are two types of angioplasty treatments. Percutaneous Transluminal Coronary Angioplasty, or PTCA, is performed by a cardiologist and is used to remove a coronary artery obstruction. Percutaneous Transluminal Angioplasty, or PTA, on the other hand, is performed by a radiologist and is used to treat other minor arteries. Typically, medical balloons applied to PTA are assembled with "Over-the-Wire" platform whereas balloons used for PTCA are assembled by "Rapid-Exchange" platform. In both platforms, the guide wire is inserted inside the internal catheter while the angioplasty balloon is folded three to six times, depending on balloon size, and rolled around the internal catheter. An external catheter is then fixed at the proximal end of the balloon. A saline solution is used to inflate the balloon during the surgery by injection inside the opening between the internal and external catheters. The two types of platforms are described in more detail below.

4.3.1.1 Over-the-Wire Platform

With this platform, the guide wire, the internal catheter, and the external catheter are all co-axial. The treatment of a patient using over-the-wire platform requires two people; one to guide the balloon and the other to inject a saline solution to inflate the balloon. This platform is usually used during PTA where the injury is very close to the catheter entry point. In the case where the lesion is far from the catheter entry point the rapid-exchange platform is preferred. A figure of the over-the-wire assembly is shown below.

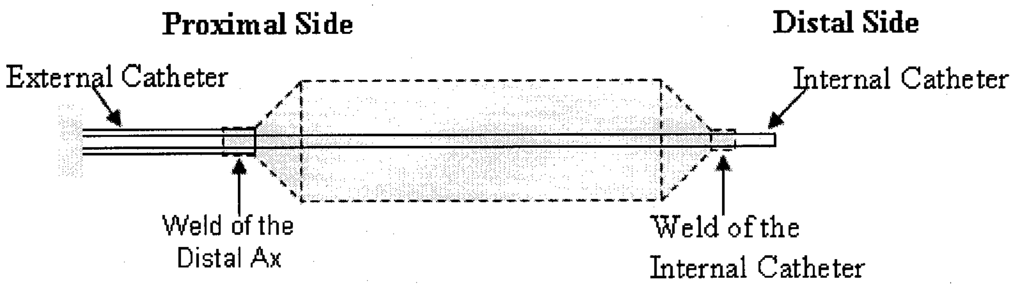


Figure 4-3 Detailed View of the Over-the-Wire Platform

4.3.1.2 Rapid-exchange Platform

The rapid-exchange platform is a modified version of the over-the-wire platform. In this platform, only the distal portion of the internal catheter is inserted inside the external catheter. An orifice permits the guide wire to exit parallel to the external catheter on the proximal portion of the assembly. This catheter assembly, usually used in PTCA, makes it possible for the treatment of coronary arteries by a single person. The assembly for the rapid-exchange platform is shown in Figure 4-4.

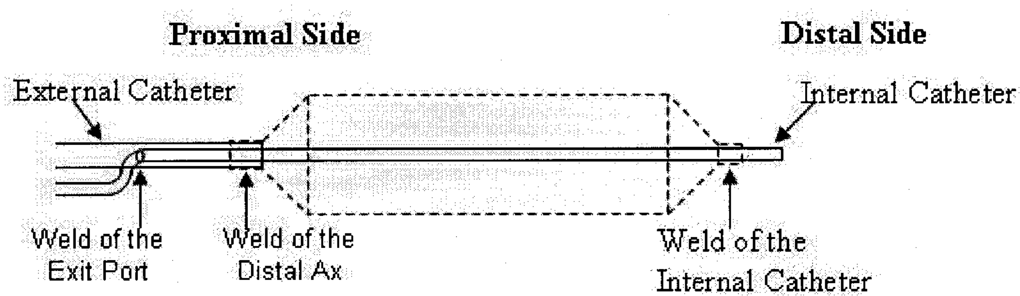


Figure 4-4 Detailed View of Rapid-Exchange Assembly

4.4 Welding the Internal Catheter and the Distal Axe

Welding the distal axe connects the external catheter to the proximal side of the balloon. Welding the internal catheter, on the other hand, connects the internal catheter to the distal side. In order to perform a proper weld, it is imperative that the material of the catheter tube be compatible with the balloon material. Compatibility implies that two materials possess similar properties such as similar melting/fusion points. If this cannot be achieved then a tolerance of 2 degrees Celsius is acceptable. It is very important to note when ordering tubing that it be annealed. Basically this process consists of heating the tubes after extrusion to allow them to release any residue accumulated inside of them during the extrusion process. The end result is a stronger tube with a higher rated burst pressure. The following figures demonstrate how the distal ax and internal catheter are welded together.

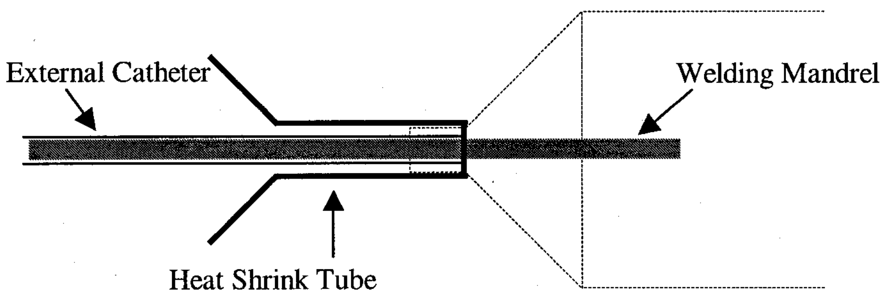


Figure 4-5 Welding the Distal Ax

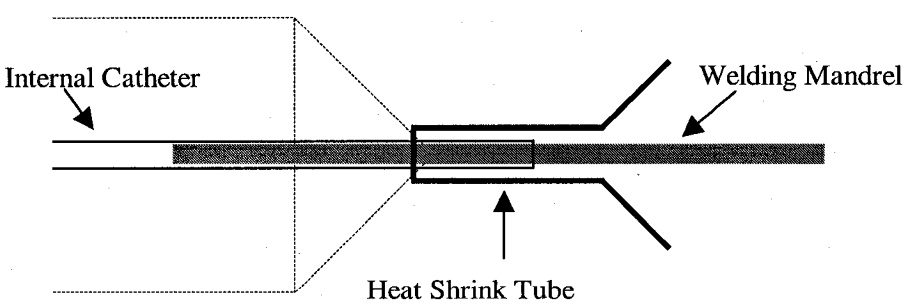


Figure 4-6 Welding the Internal Catheter

When heated, the heat shrink tube, made from a compound called Fluorinatedethylenepropylen, exerts pressure on the internal and external catheters and on the balloon necks. With pressure applied evenly by the shrinking tube, the resulting weld is usually very smooth and reliable.

The welding mandrel serves to avoid collapse while the pressure is applied. The mandrel provides some much needed rigidity during the fusion process since most plastic materials, if unsupported, soften and sag at higher temperatures.

4.5 Inspection of the Weld

All welded assemblies are thoroughly inspected to ascertain conformity with accepted standards. The first stage of the inspection is basically a visual examination of the weld and the identification of possible visual defects. Assembly units that pass the visual are then subjected to rigidity, sealing, and burst pressure tests. Table 4-1 lists the quality control tests associated with balloon assembly.

Inspection	Distal Shaft	Internal Catheter	Exit Port
Visual Inspection	☑	☑	☑
Rigidity	☑	☑	
Sealing	☑	☑	☑
Burst Pressure	☑	☑	☑

Table 4-1 Welding Inspection Checks

4.5.1 Visual inspection

A visual inspection is done with the aid of a microscope. A good weld is virtually invisible. If defects are found, such as the appearance of bubbles or other flaws at the joints, it suggests that the material was heated at too high a temperature or possibly for too long.

4.5.2 Rigidity Test on Balloon Assembly

The rigidity test is performed by pinching the welding point with the finger and thumb while pressing down on the end. A catheter that folds exactly at the welding point implies that the material is too weak. To correct this weakness the welding temperature or the welding time need to be dropped.

4.5.3 Sealing Test

The sealing test requires a syringe. With the aid of a syringe inject water inside the balloon to detect any possible leaks. An alternate method requires the balloon to be filled with air using an empty syringe while keeping it submerged in water. Bubbles escaping at the joints are a clear indication that the balloon has a leak.

4.5.4 Burst Pressure Test

The burst pressure is measured to ensure that the welding strength exceeds the minimum safety and reliability standards for angioplasty procedures. The rated burst pressure of each weld, particularly that of the distal axe, must be higher than that of the balloon. The nominal burst pressure posted on the packing of commercial balloons corresponds to the pressure applied into the balloon assembly during surgery. Statistically, at least 99.9% of the balloons will not burst when they are subjected to a pressure lower or equal to the nominal rupture pressure.

After the weld quality tests are completed, the balloon is then sterilized and packaged for distribution.

4.6 Surgical Procedure

Percutaneous Transluminal Coronary Angioplasty surgery is usually performed under local anesthesia so that the doctor may ask the patient if they feel any pain or awkwardness during surgery. A thin guide catheter is entered into the blood vessel through the femoral artery located at the top of the leg as shown in the Figure 4-7 [18].

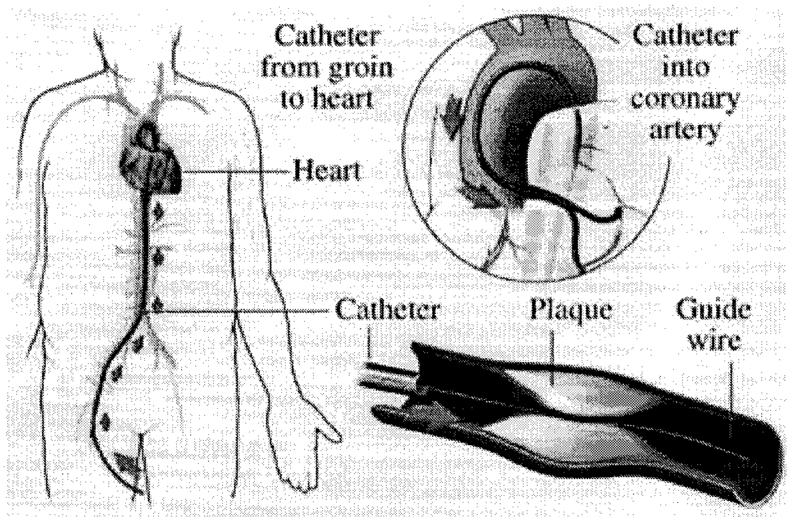


Figure 4-7 Insertion of Balloon Catheter through the Femoral Artery (Permission granted by Nucleus Medical Art)

The catheter, which is almost one meter in length, is fed through blood vessels and finally into the coronary artery. The physician is able to monitor the location of the catheter by injecting a dye and monitoring its location with the aid of an x-ray base fluoroscope machine. When the guide catheter reaches its destination, a guide wire, which is approximately the thickness of a pencil lead, is then threaded through the guide catheter to the lesion site. With the guide wire in place, the balloon catheter is then advanced to the clogged artery and inflated for a few seconds. If no pain is felt by the patient, the surgeon proceeds to inflate the balloon for an entire minute forcing the plaque against the arterial walls and allowing for proper blow flow. The catheter is then removed.

At the discretion of the operating surgeon, a stent, made of stainless steel, is sometimes planted within a dilated artery to prevent stenosis from re-occurring. The stent opens up and locks into place once the balloon inflates fully within the artery, shown in Figure 4-8 [20].

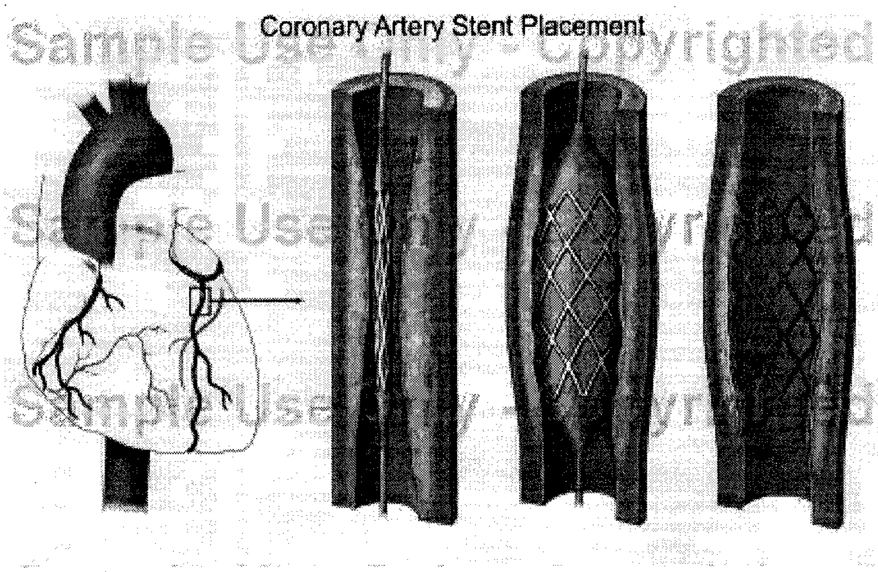


Figure 4-8 Artery before and after stent expansion (Permission granted by Nucleus Medical Art)

Recovery time for PTCA surgery usually ranges from a couple of weeks to a month, a considerably shorter time than traditional bypass surgery. However PTCA does have its setbacks. Almost half the patients who undergo this procedure will require a second intervention. Doctors are currently working on possible ways to reduce arterial wall buildup after the initial PTCA procedure.

PTCA surgery has seen exponential growth and incredibly, in the late 1990s, it has been performed on over one-half million people.

4.6.1 Cost of Surgery

A person suffering from stenosis these days can choose one of many methods to treat or reduce heart disease such as heart bypass surgery or the less invasive PTCA procedure. But how does one weigh which method is better in the long term?

According to Dr. Mark A. Hlatky, a professor of health research and policy at Stanford University School of Medecine, the choice should be based on the severity of the problem. He states, "I would now tend to recommend bypass surgery for patients with three blocked vessels, and angioplasty for patients with one blocked vessel. In patients with two blocked vessels who can be treated with either angioplasty or surgery, the medical results are so close that how the patient feels about the two options should be given the most weight in the decision"[27]. However he later states, "They're both good procedures in the hands of experienced doctors" [27].

The decision should also depend on how the patient will react to open heart bypass surgery, as Dr. Hlatky says, "The chance of complete angina [chest pain from heart disease] relief and improvement in physical capacity is somewhat better with bypass surgery, but at the price of more initial discomfort, a longer hospital stay and longer recovery time" [27].

Earlier studies stated that angioplasty procedures are safer and much cheaper than the traditional heart surgery. However new studies have shown that over half the patients having opted for PTCA will have to either return for a second angioplasty or need a bypass surgery. Dr. Hlatky states, "Even so, in the long run, angioplasty costs less than bypass surgery for patients with one or two blocked vessels, but costs about the same as bypass surgery in patients with three blocked vessels. Both methods were comparable in terms of overall rates of death and subsequent heart attacks" [27].

According too the January 9th edition of New England Journal of Medicine, co-written by Dr. Hlatky, the cost of angioplasty (21 113$US) is initially much cheaper than bypass surgery (32 347$US). However, over a five year span, the cost of health care for angioplasty (56 225$US) almost equalled that of heart surgery (60 918$US). He finally concludes by stating, “Balloon angioplasty (52 930$US) has a significant cost advantage over bypass surgery (58 498$US) in two-vessel coronary disease, but the costs are similar in three-vessel disease (59 430$US for surgery vs. 60 918$US for angioplasty)” [27].

5 MODELING RESULTS

This thesis aims to reduce the time spent on research and development of angioplasty balloon production. Balloons are still made using trial-and-error methods depending on BFM operator experience. With the implementation of a cycle-to-cycle controller this process can be significantly reduced. David Yannes, an employee of Interface Associates Inc., believes that most balloon manufacturing companies take months or evens years before attaining a balloon suitable for PTCA surgery.

To reduce or possibly eliminate material and time invested in the R&D phase, a model of balloon fabrication sequences is needed. With a better understanding of how the outputs relate to the inputs, a controller can be designed for the Balloon Forming Machine. A well tuned controller will increase productivity, waste less material, and save more energy.

5.1 Chosen Inputs and Outputs

A total of five inputs and four outputs will be analyzed and used to make a model. The selected inputs are: *applied pressure*, *mold temperature*, *heating time*, *stretch distance*, and *parison length*. The outputs to be controlled and measured are: maximum rated *burst pressure*, *wall thickness*, *balloon compliance*, and *balloon quality*. Thus, we would like to know how the controllable inputs affect the performance parameters as shown in Table 5-1.

	Controllable Inputs		Performance Parameters
DES	Parison Length	AFFECT	Wall Thickness
BFM	Applied Pressure		Burst Pressure
BFM	Mold Temperature		Compliance
BFM	Heat Time		Balloon Quality
BFM	Stretch Distance		

Table 5-1 Input/Output Relation

5.2 Importance of Output Parameters

The results from measuring output parameters such as balloon compliance, wall thickness and maximum rated burst pressure are all equally important in angioplasty balloons. Each parameter has a specific role to play during surgery to clear an artery. If any one parameter fails, Percutaneous Transluminal Coronary Angioplasty surgery cannot be successful.

It is important to note that the standard units of measure for the BFM are British Imperial. Test results from the BFM are recorded in Imperial Units with the equivalent SI units in parentheses.

5.2.1 Rated Burst Pressure

A high rated burst pressure is one crucial output parameter. Should an angioplasty balloon burst before being inflated to its nominal pressure, proper arterial dilatation and stent expansion could not be possible. More specifically, a stent used on 3 x 15 mm angioplasty balloons will only expand and lock in place within the artery once the balloon expands to a diameter larger than 3 mm. In balloons that rupture before reaching the desired size, the stent will not open and the procedure will again have to be repeated with another balloon. An ideal burst pressure for 3 x 15 mm balloons is from 22 to 24 atmospheres (2.23 to 2.43 MPa), whereas 8 x 30 mm balloons usually rupture in the 16 to 18 atmosphere range (1.62 to 1.82 MPa).

5.2.2 Balloon Wall Thickness

Balloon wall thickness also plays a large role in balloon performance. When a balloon is mounted on a balloon catheter, it is usually folded three to six times like an umbrella, in order to reduce its profile to a size that will facilitate insertion into the artery. If a balloon is too thick it will be discarded. Thick-walled balloons have poor folding qualities and usually result in a profile that is too large for assembly to the balloon catheter. Balloon walls that are too thin, on the other hand, will have a burst pressure rating that is too low and unacceptable.

Thickness distribution is another factor that needs to be considered. Balloons expanded with an uneven wall thickness are equally unacceptable since they too have inferior burst pressure ratings. Furthermore, balloons with an uneven wall thickness will not fold properly and thus should be discarded.

An ideal single-wall thickness for 3 x 15 mm angioplasty balloons ranges from 0.1778 to 0.1905 mm while for larger 8 x 30 mm balloons, a value of 0.474 to 0.508 mm is the norm

5.2.3 Balloon Compliance

Balloon compliance is found by measuring the final diameter of the balloon before rupture. Depending on the selected inputs the final diameter of 3 x 15 mm balloons can vary from 3.5 to 4.2 mm. It is important to remember that balloon compliance is inversely related to wall thickness. The challenge then is to find the best trade-off between uniform wall thickness and compliancy.

5.2.4 Physical Properties

Physical properties are qualitative results rather than quantitative. The verification of an angioplasty balloon for physical defects is always done before moving on to take measurements. Balloons with physical defects such as crow feet or radial rings are considered as rejects and should immediately be discarded.

5.2.4.1 Crow Feet

Crow feet form on the part of the balloon where the cone transitions into the neck. This non conformity occurs when the Balloon Forming Machine stretches the tube before it has a chance to expand and fill the cavity of the center mold. An example of crow feet is portrayed in the picture taken below during one of the experiments.

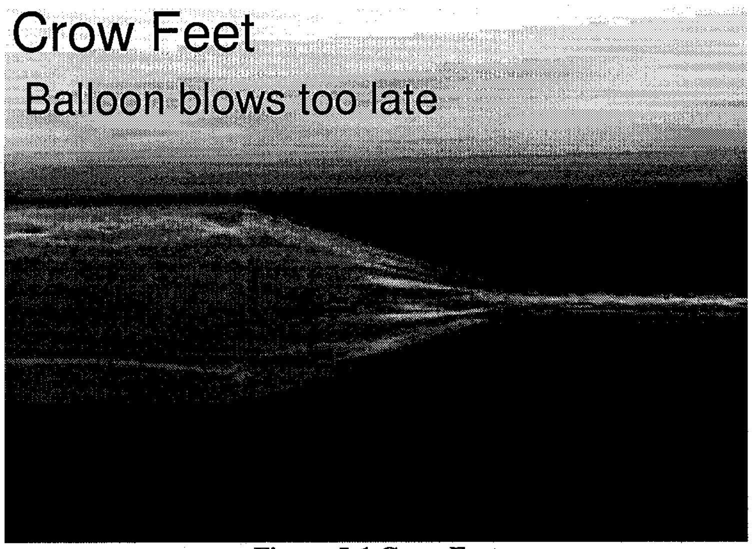


Figure 5-1 Crow Feet

Most crow feet formations can be solved either by increasing the applied pressure, the heating time, and/or the mold temperature.

5.2.4.2 Radial Rings

Radial rings also occur on the cones of the balloon. This defect emerges when an angioplasty balloon blows too early before the Balloon Forming Machine has a chance to apply stretching. As a result the balloon is forced into the end-plugs creating the radial rings shown in Figure 5-2.

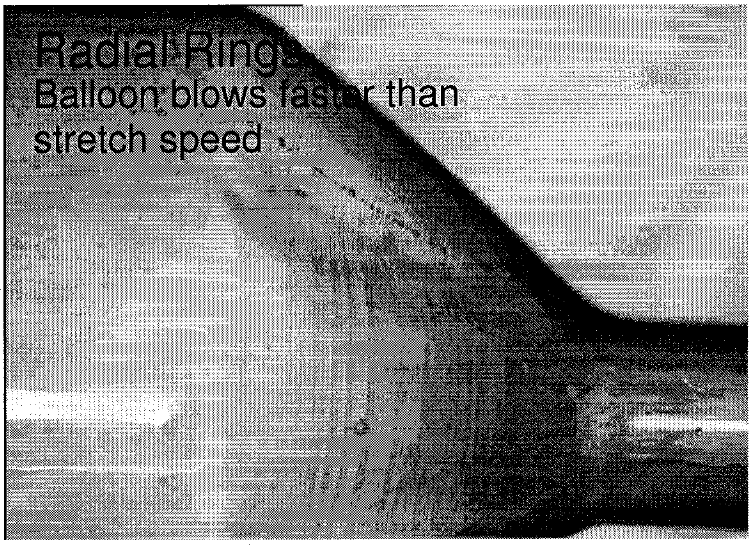


Figure 5-2 Radial Rings

Radial rings can be eliminated by decreasing the applied pressure, the heating time, and/or the mold temperature.

5.3 Fabricating and Testing Balloons

The following sections show and explain the results obtained from various tests performed on 3 x 15 mm and 8 x 30 mm angioplasty balloons.

5.3.1 3 X 15 mm Angioplasty Balloon Tests

Fifty to sixty tests were done to determine the input-output relationships on the Balloon Forming Machine for 3 x 15 mm angioplasty balloons. Table 5-2 shows the input selection for these tests. The graphs in this chapter reflect the values resulting from the change of a single input on *one* balloon. Any balloons that had erroneous output results such as a really low burst pressure were duplicated.

Applied Pressure (atm)	10 (1A)	15 (1B)	20 (1C)	25 (1D)	27 (1E)	29 (1F)	31 (1G)	33 (1H)	**35 (1I)**	37 (1J)	39 (1K)	41 (1L)
Forming Temp. (deg C)	35 (2A)	40 (2B)	45 (2C)	50 (2D)	55 (2E)	**60 (2F)**	65 (2G)	70 (2H)	75 (2I)	80 (2J)	85 (2K)	-
Forming Time (s)	35 (3A)	40 (3B)	45 (3C)	50 (3D)	55 (3E)	**60 (3F)**	65 (3G)	70 (3H)	75 (3I)	80 (3J)	-	-
Stretch Distance (mm)	8.5 (4A)	9.5 (4B)	10.5 (4C)	11.5 (4D)	12.5 (4E)	**13.5 (4F)**	14.5 (4G)	15.5 (4H)	16.5 (4I)	17.5 (4J)	-	-
Parison Length (mm)	11 (5A)	12 (5B)	13 (5C)	14 (5D)	**15 (5E)**	16 (5F)	17 (5G)	18 (5H)	19 (5I)	20 (5J)	-	-

Table 5-2 Testing 3 x 15 mm balloons

The values in the grey shaded cells are the inputs which appear to produce the best balloons. In other words a mold with an internal applied pressure of 35 atmospheres (3.55 MPa), set to a temperature of 60°C (333 K) for 60 seconds, with a stretch distance of 13.5 mm at each side and a parison length of 15 mm will likely produce a balloon with superior performance parameters.

In order to observe the impact of any one input on the output, one input is varied while the remaining four remain constant. The test technician might keep the mold temperature, heat time, stretch distance, and parison length constant while varying the applied pressure from 10 (referenced as 1A) to 41 atmospheres (1L) and recording the results. The process is then repeated but this time by varying the mold temperature (2A to 2K from Table 5-2) and so forth.

5.3.2 8 X 30 mm Angioplasty Balloon Tests

The 8 X 30 mm balloons were tested in the same manner as the smaller balloons. Once again the values in the shaded boxes in Table 5-3 represent those inputs that yield the best results.

Applied Pressure (atm)	18 (1A)	20 (1B)	22 (1C)	**24 (1D)**	26 (1E)	28 (1F)	30 (1G)
Forming Temp. (deg C)	40 (2A)	50 (2B)	60 (2C)	**70 (2D)**	80 (2E)	90 (2F)	100 (2G)
Forming Time (s)	110 (3A)	120 (3B)	130 (3C)	**140 (3D)**	150 (3E)	160 (3F)	170 (3G)
Stretch Distance (mm)	24 (4A)	26 (4B)	28 (4C)	**30 (4D)**	32 (4E)	34 (4F)	36 (4G)
Parison Length (mm)	19 (5A)	21 (5B)	23 (5C)	**25 (5D)**	27 (5E)	29 (5F)	31 (5G)

Table 5-3 Testing 8 x 30 mm balloons

5.4 Interpretation of Results

The graphs in this section are the results obtained from the tests performed in the CNRC-NRC IMI biomedical laboratory. These graphs contain enough information to help design a cycle-to-cycle controller capable of relating the outputs to the selected inputs.

5.4.1 The 3 X 15 mm Angioplasty Balloon

For each of the five input parameters, graphs are divided into two sections; quantitative results and qualitative results. As previously noted, quantitative results include balloon burst pressure, wall thickness and balloon compliance, whereas the qualitative results assess physical defects and material thickness distribution.

5.4.1.1 Applied Pressure Variation

The first input analyzed was the applied pressure into the balloon mold. This input was augmented from 10 atmospheres to 41 atmospheres (1.01 to 4.15 MPa) while other input parameters remained unchanged.

5.4.1.1.1 Quantitative Results

The application of different pressures into the mold can have significant effects on balloon characteristics. The graphs below show that an increase in applied pressure leads to an increase in burst pressure and balloon compliance while balloon wall thickness actually decreases. The decrease in wall thickness occurs when the augmented applied pressure forces more rapid expansion and increased material stretching.

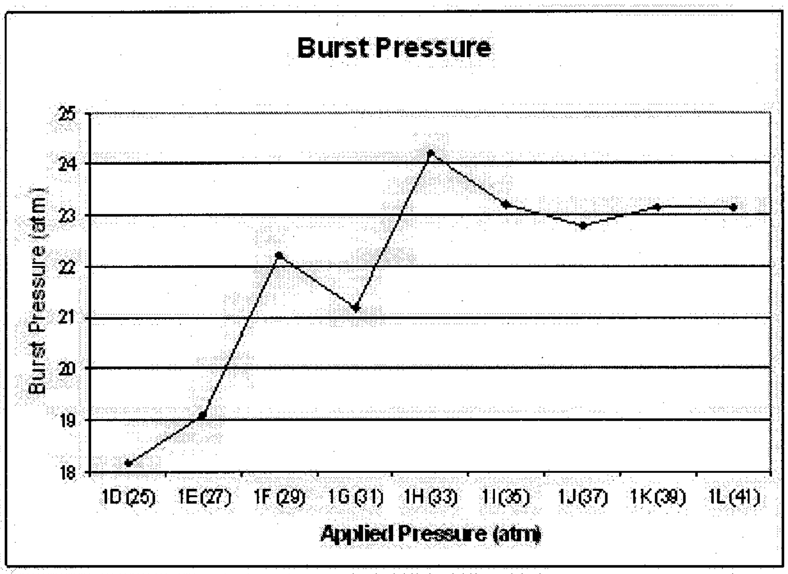


Figure 5-3 Burst Pressure as a Function of Applied Pressure

Burst pressure and balloon compliance are measured with the aid of a deployment tester. The deployment tester injects a solution into the balloon to increase the pressure within the balloon in increments of one atmosphere. The figure 5-4 shows a photograph of the deployment tester.

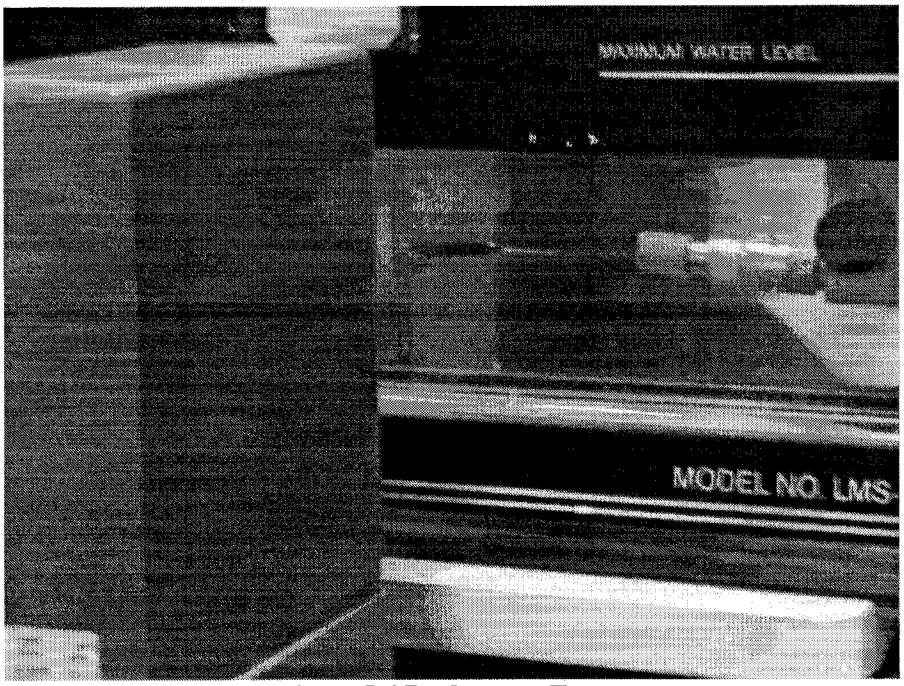


Figure 5-4 Deployment Tester

A laser emitting from the deployment tester measures a balloon's diameter before bursting.

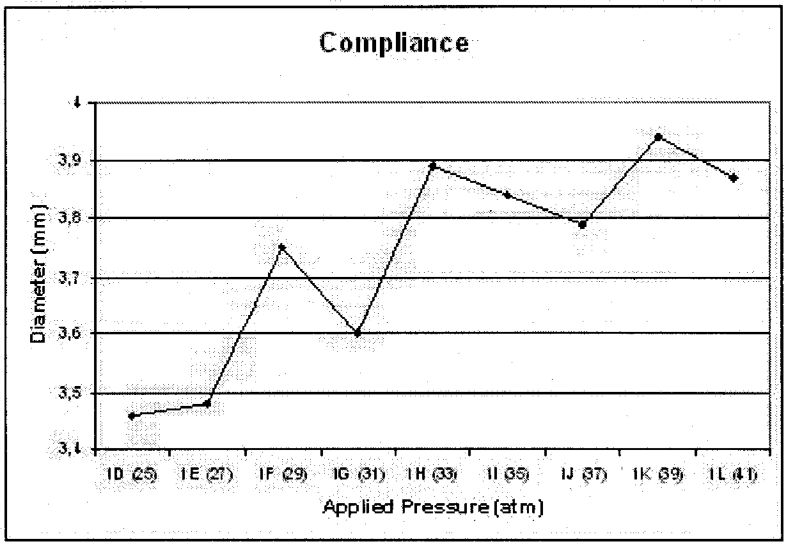


Figure 5-5 Compliance as a Function of Applied Pressure

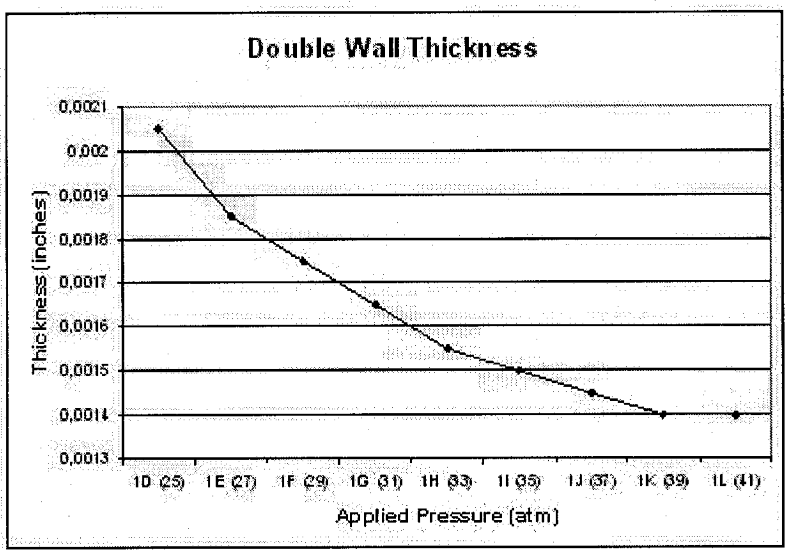


Figure 5-6 Wall Thickness as a Function of Applied Pressure

5.4.1.1.2 Qualitative Results

All angioplasty balloons are verified for physical defects and thickness distribution. Table 5-4, supplied by Zoe Sarrat-Cave, is a legend used to indicate a balloon's physical condition. A nil score indicates a perfect balloon with no visible defects; whereas a score of three indicates a balloon with major defects. When no balloon is formed from the selected input parameters a value of four is assigned.

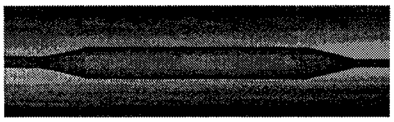
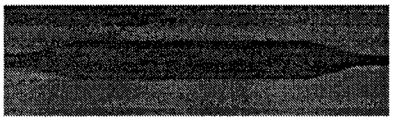
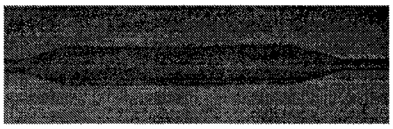
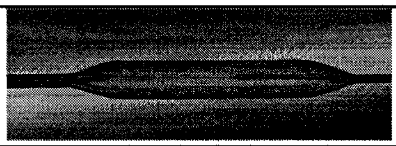
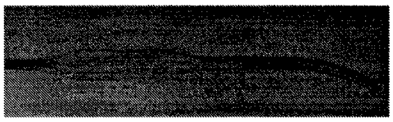
Score	Criteria	Sample
0	**The balloon has no visible defects.**	
1	**The balloon contains minor defects:** crow feet may be visible but do not surpass more that 50% of the length of the cone, no axial lines are visible.	
2	**The balloon contains some major defects:** crow feet surpass more than 50% of the length of the cones, no axial lines are visilbe.	
3	**The balloon contains many major defects:** crow feet are visible in the body of the balloon, and/or one or more axial lines are present.	
4	**No balloon was formed.** The balloon forming sequence did not produce a balloon.	

Table 5-4 Balloon Quality Legend

Figure 5-7 shows the results obtained on balloon quality when varying applied pressure. A suitable balloon is formed in between 33 and 39 atmospheres (3.34 to 3.95 MPa).

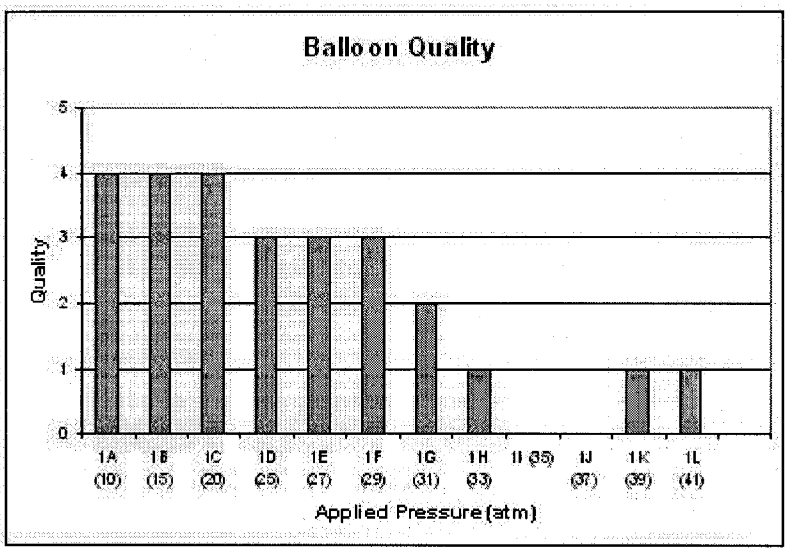
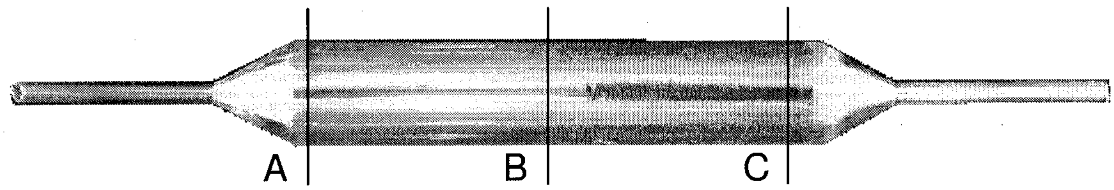


Figure 5-7 Balloon Quality as a Function of Applied Pressure

A similar legend shown in Table 5-5 is used to rate a balloon's wall thickness distribution. A score of zero indicates an even thickness distribution which is desirable in angioplasty balloons. A score of two means a balloon has significantly different thicknesses at the three measured points A, B, and C.



Score	Criteria
0	**The balloon wall thickness is evenly distributed:** considered identical, ≤0.00005" difference between measurements
1	**The balloon wall thickness is fairly evenly distributed:** ≤0.0002" difference between the measurements
2	**The balloon wall thickness is not evenly distributed:** >0.0002" difference between the measurements

Table 5-5 Thickness Distribution Legend

The instrument used to measure the thickness is a micrometer seen in Figure 5-8.

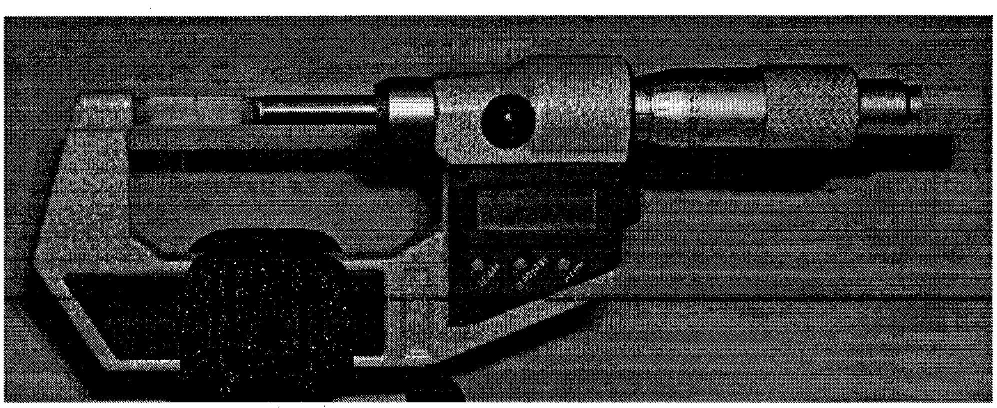


Figure 5-8 Micrometer Used to Measure Balloon Wall Thickness

According to Figure 5-9, a balloon with even material distribution can be expanded when the applied pressure is set within the range of 31 to 39 atm (3.14 to 3.95 MPa).

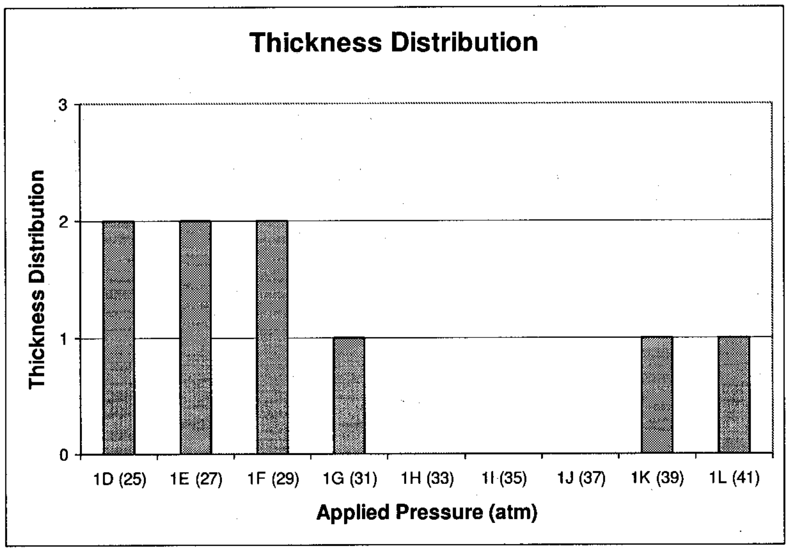


Figure 5-9 Material Distribution As a Function of Applied Pressure

5.4.1.2 Mold Temperature Variation

The next input is the temperature of the mold before the tubing is stretched. In this experiment the mold temperature is varied from 35 to 85 degrees Celsius (308 to 358K).

5.4.1.2.1 Quantitative Observations

As in the first case, the balloon's compliance and rated burst pressure go up, while the walls tend to thin out with an increase in temperature. Generally balloon compliance and wall thickness are inversely related. As seen in the Figures 5-11 and 5-12, a thinner balloon wall will usually result in a greater compliance.

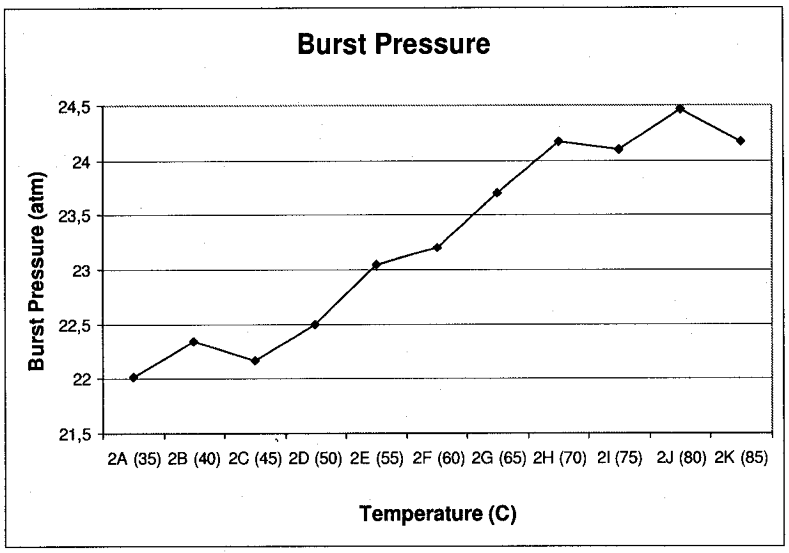


Figure 5-10 Burst Pressure as a Function of Mold Temperature

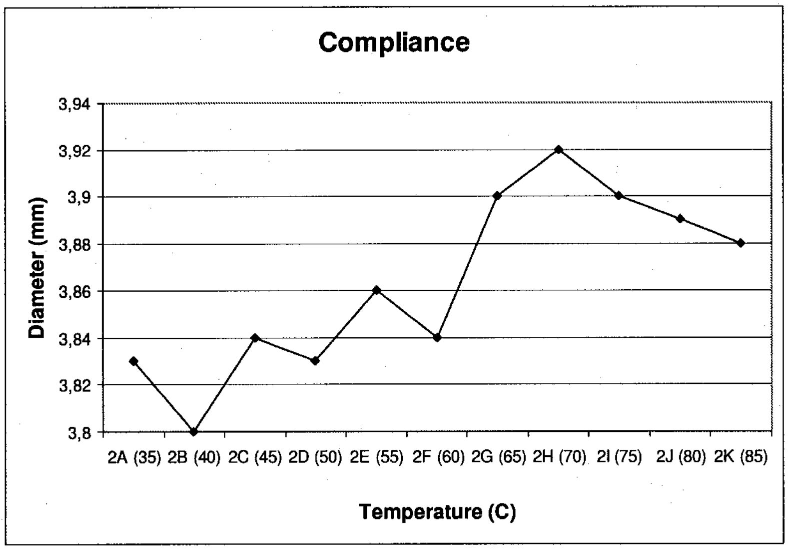


Figure 5-11 Compliance as a Function of Mold Temperature

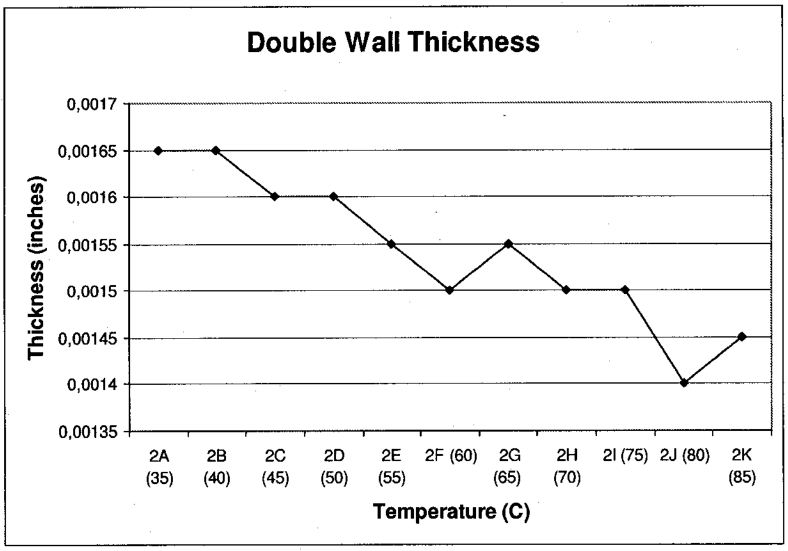


Figure 5-12 Wall Thickness as a Function of Mold Temperature

5.4.1.2.2 Qualitative Observations

Conforming balloons are obtained most frequently when the molds are operated within a temperature range of 55 to 65°C (328 to 338 K).

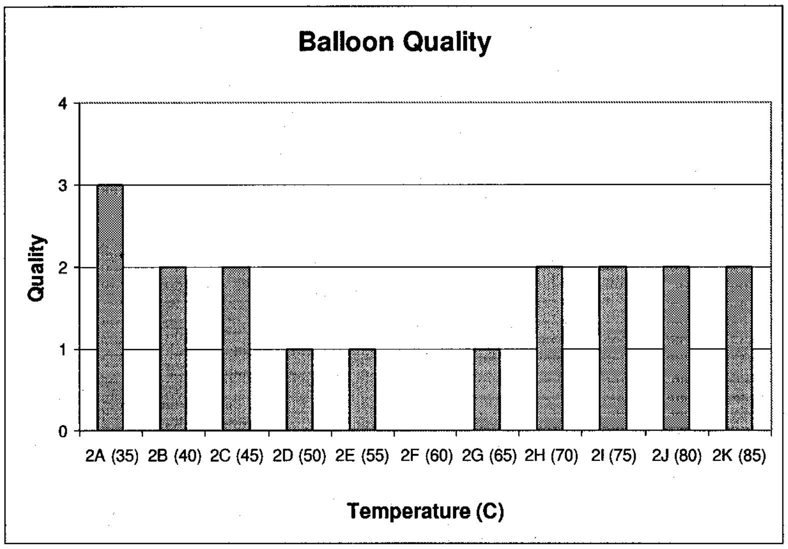


Figure 5-13 Balloon Quality as a Function of Mold Temperature

Angioplasty balloons with an even thickness distribution also are most frequently obtained within a similar temperature range as seen in Figure 5-14.

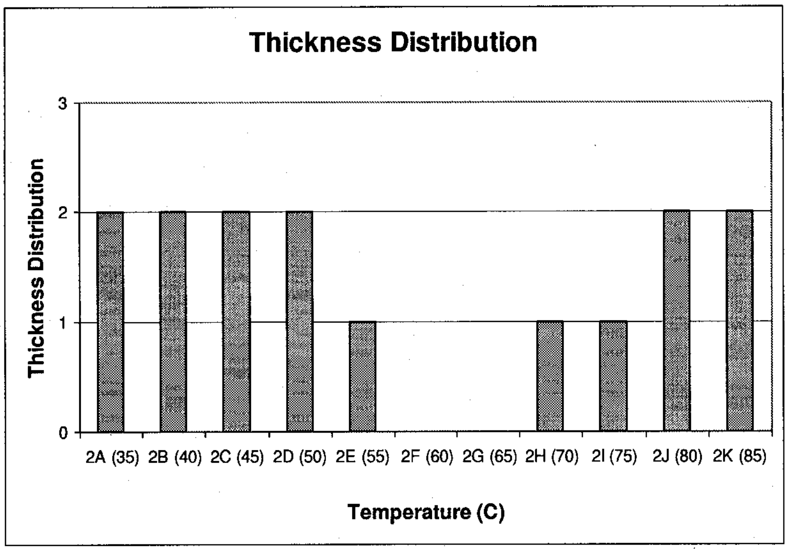


Figure 5-14 Material Distribution as a Function of Mold Temperature

5.4.1.3 Heat Time Variation

The next input parameter is the heating time. In this case the input ranges from 35 to 80 seconds.

5.4.1.3.1 Quantitative Observations

The plotted points in the following graphs suggest that the longer a material is heated before the stretching and forming stages, the thinner the wall thickness becomes and the lower the maximum rated burst pressure.

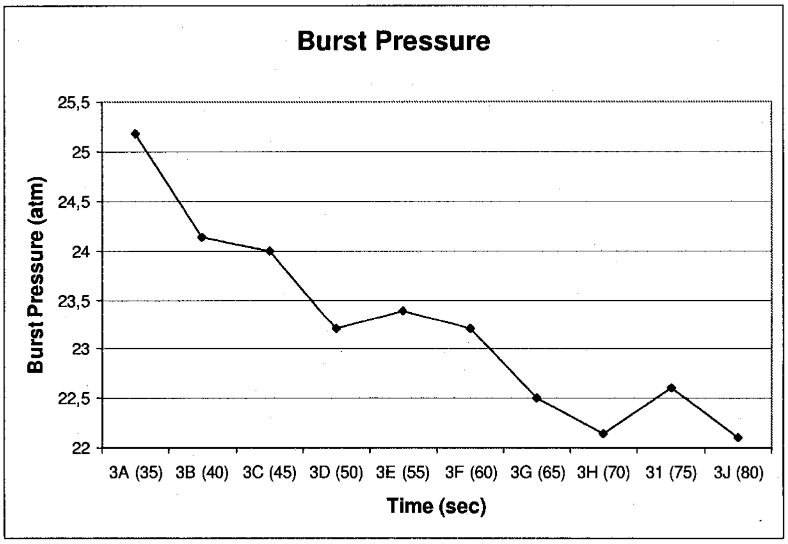


Figure 5-15 Burst Pressure as a Function of Heat Time

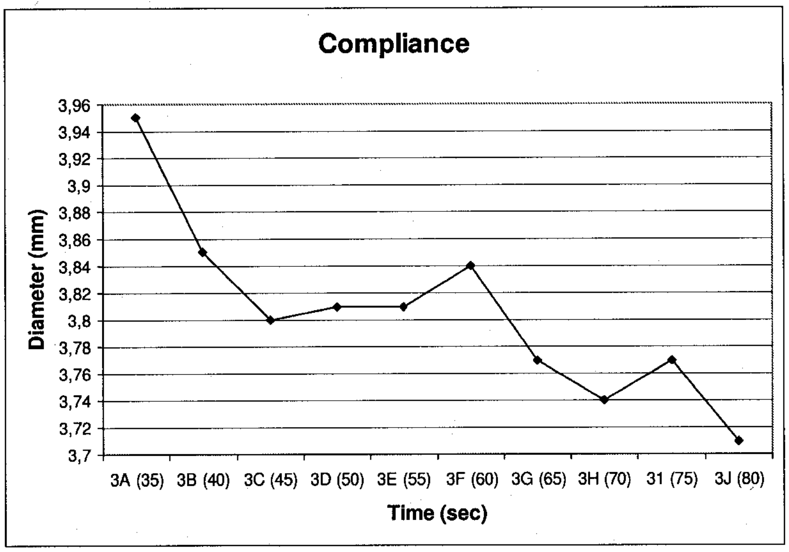


Figure 5-16 Compliance as a Function of Heat Time

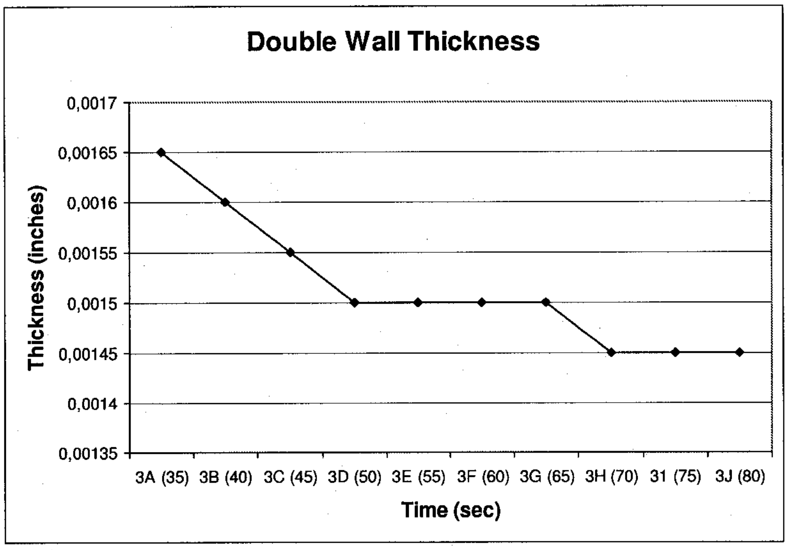


Figure 5-17 Wall Thickness as a Function of Heat Time

Looking at Figure 5-17 one would expect Figure 5-16 to increase in value as the heat time goes up. However that is not the case here. One possible explanation could be that the walls are so thin that they can no longer stretch without the balloon bursting.

5.4.1.3.2 Qualitative Observations

When the other four input parameters are held constant a balloon free of defects forms most frequently when the heat time is within 50 to 65 seconds.

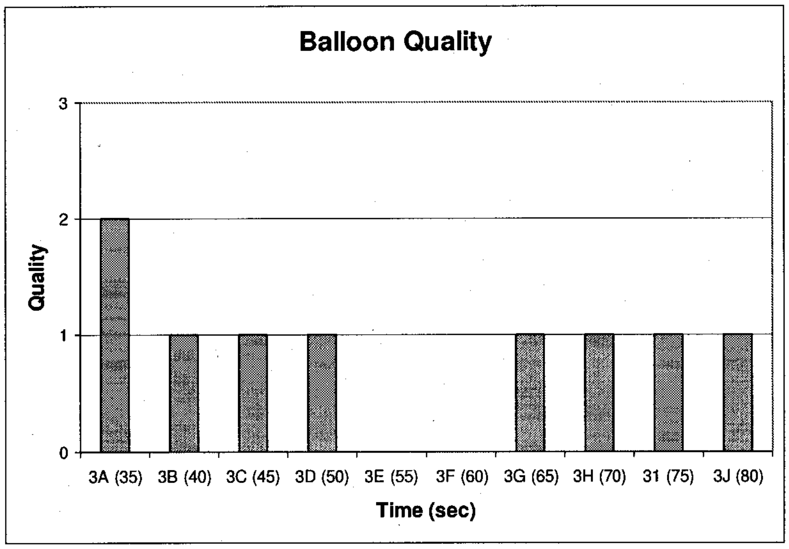


Figure 5-18 Balloon Quality as a Function of Heat Time

Figure 5-19 indicates that a balloon with the most consistent wall thickness distribution throughout the body is formed when the heat time ranges from 50°C to 70°C (323 to 343K).

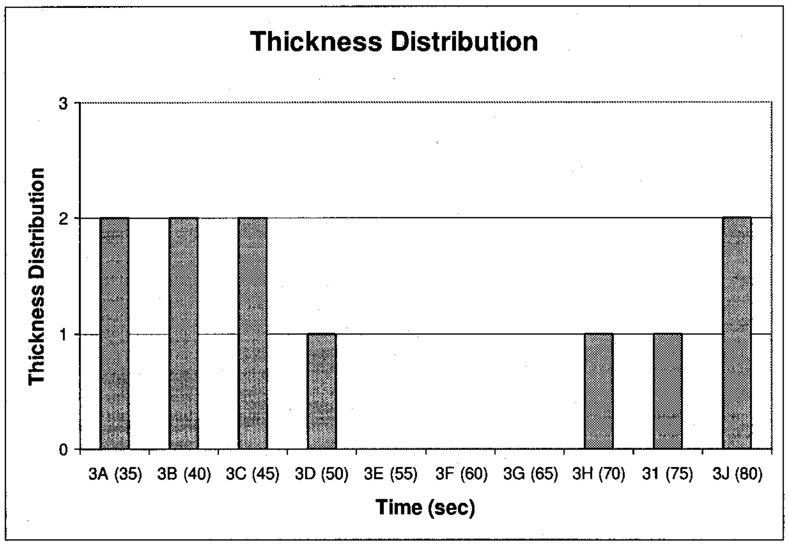


Figure 5-19 Material Distribution as a Function of Heat Time

5.4.1.4 Stretch Distance Variation

The stretch distance applied on the tubing after heating is another input parameter that deserves close analysis. A stretch ranging from 8.5 to 17.5 mm on both ends of the tubing is varied while keeping all other inputs constant.

5.4.1.4.1 Quantitative Observations

All values tend to decrease with an increase in stretch distance. A longer stretch increases the thinning of a balloon's average wall thickness and causes a corresponding reduction in burst pressure.

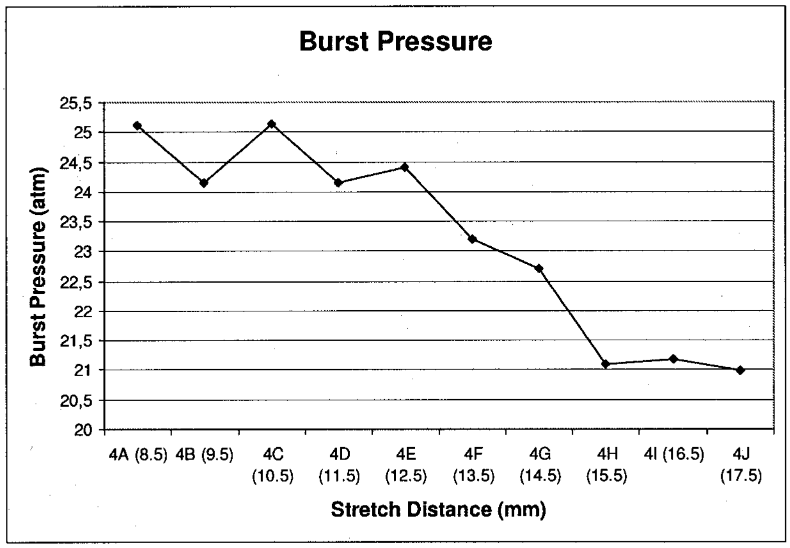


Figure 5-20 Burst Pressure as a Function of Stretch Distance

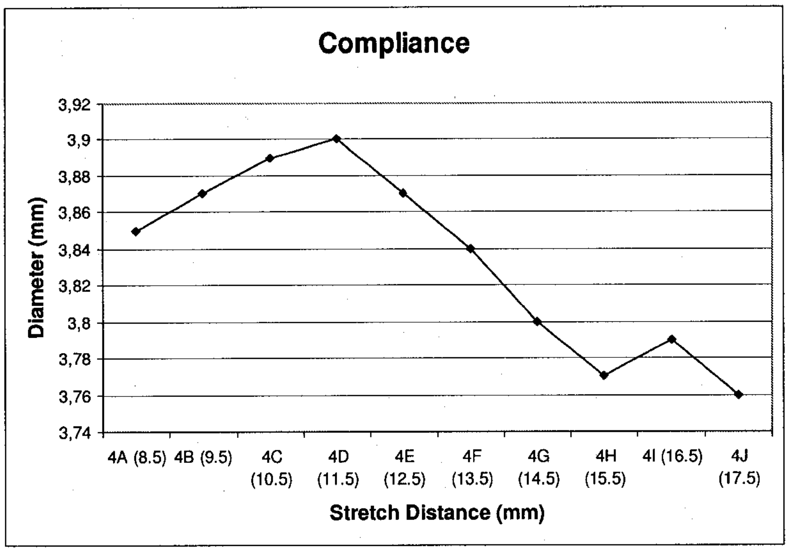


Figure 5-21 Compliance as a Function of Stretch Distance

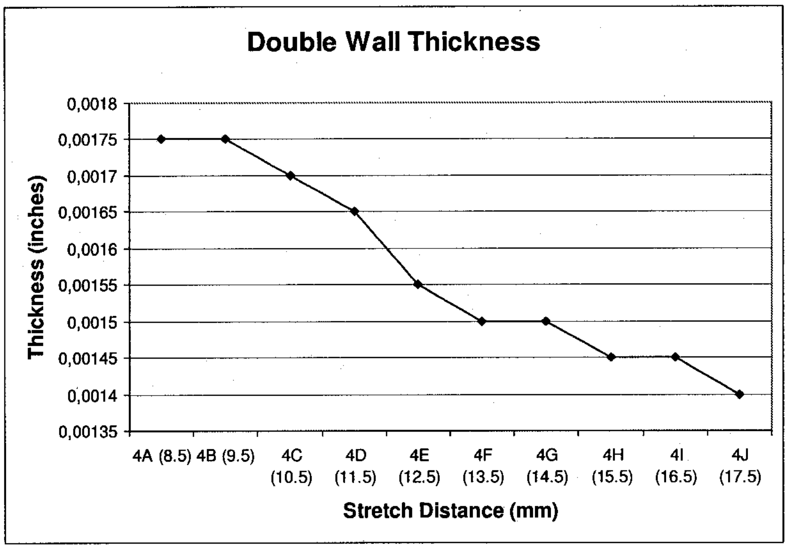


Figure 5-22 Wall Thickness as a Function of Stretch Distance

5.4.1.4.2 Qualitative Observations

The highest quality balloons are produced when the stretch distance is set in between 12.5 and 15.5 mm at each end, shown in Figures 5-23.

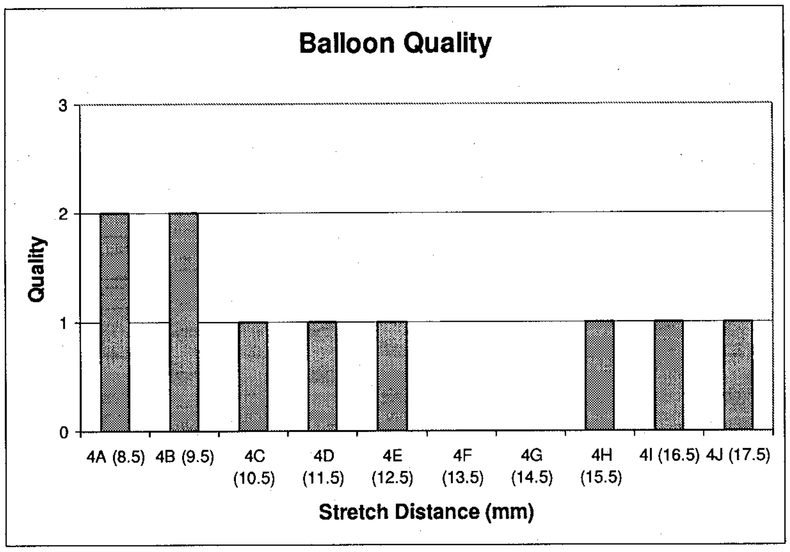


Figure 5-23 Balloon Quality as a Function of Stretch Distance

A well stretched balloon generates an even material distribution throughout its length when the stretch distance is maintained between 12.5 to 16.5 mm. See Figure 5-24.

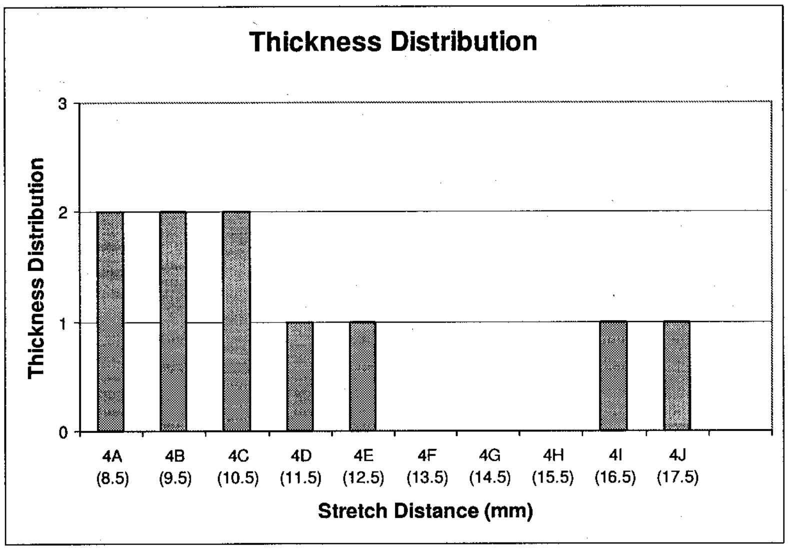


Figure 5-24 Material Distribution as a Function of Stretch Distance

5.4.1.5 Parison Length Variation

The final input to look at is the parison length. Tubing with various parisons ranging from 11 to 20 mm in length was tested with all other input left the same.

5.4.1.5.1 Quantitative Observations

The results of the tests have shown that longer parisons lead to higher burst pressure and higher balloon compliance while the wall thickness varies very little throughout the entire range.

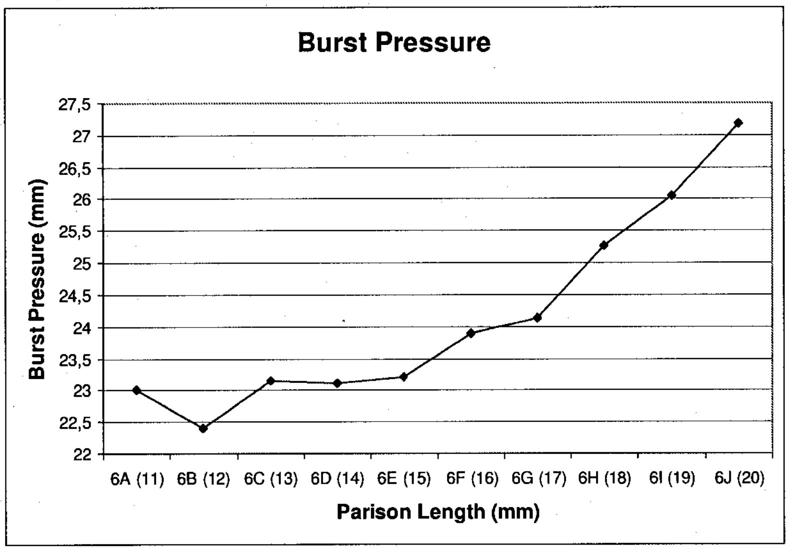


Figure 5-25 Burst Pressure as a Function of Parion Length

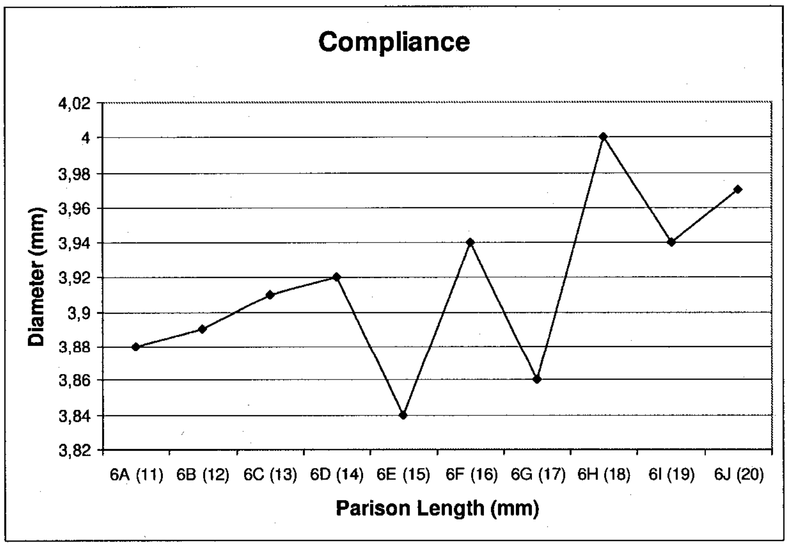


Figure 5-26 Compliance as a Function of Parison Length

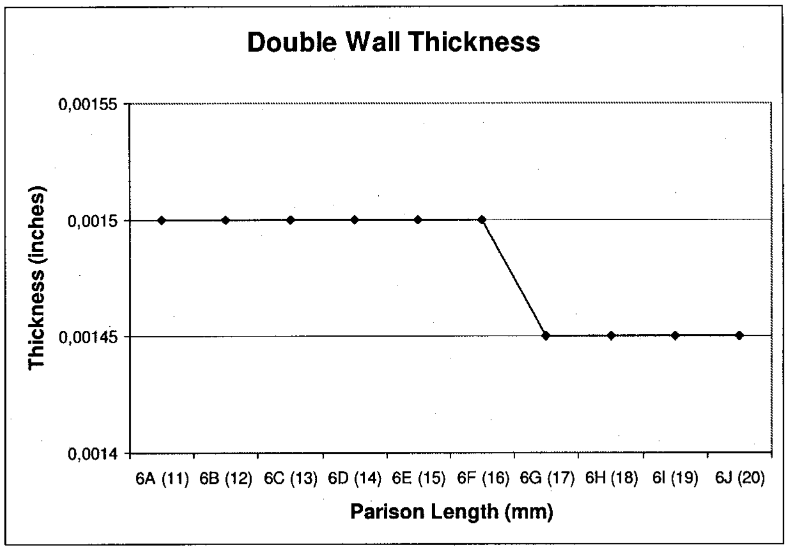


Figure 5-27 Wall Thickness as a Function of Parison Length

5.4.1.5.2 Qualitative Observations

Parison length appears to have less impact on balloon quality than the other input parameters. Figure 5-28 shows a good balloon forms when parison lengths are in between 13 and 19 mm.

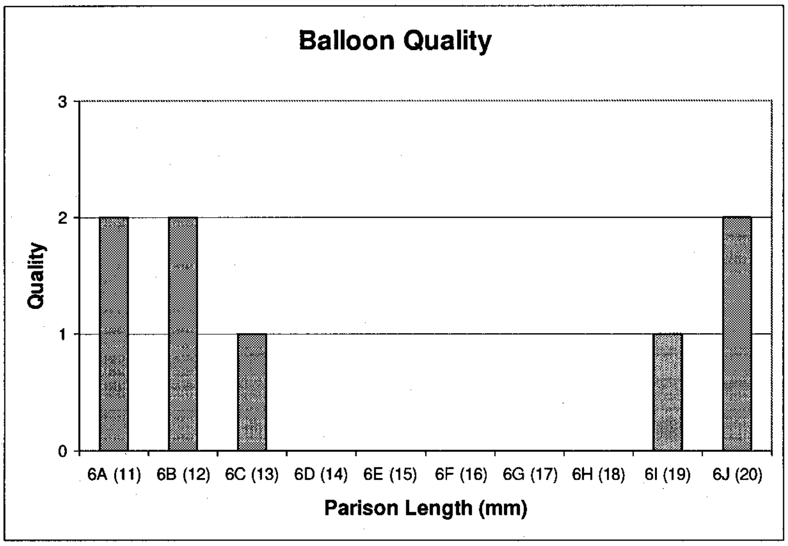


Figure 5-28 Balloon Quality as a Function of Parison Length

An even thickness distribution is found within the range of 13 to 18 mm.

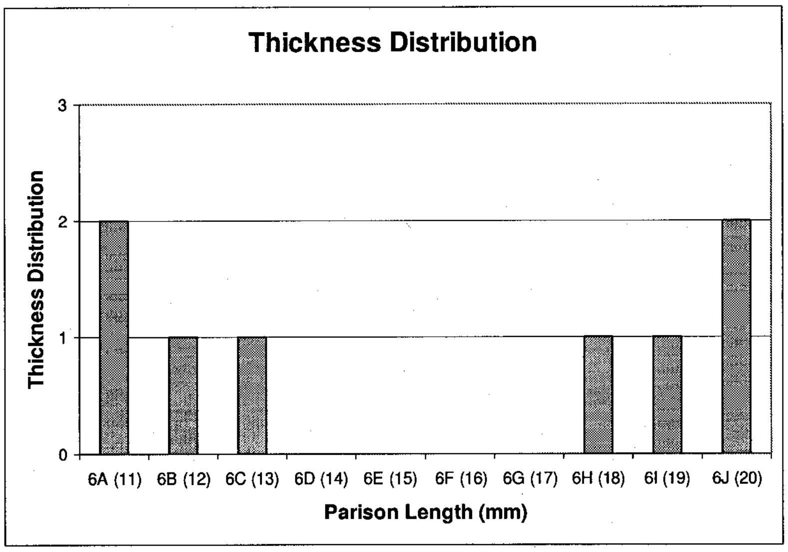


Figure 5-29 Material Distribution as a Function of Parison Length

5.4.2 The 8 X 30 mm Angioplasty Balloon

A second series of tests were done on the larger 8 x 30 mm angioplasty balloons. The selected input parameters were again varied one at a time while keeping the other four constant. The purpose for the repetition of the tests for the larger balloon is to determine if different balloon sizes exhibit similar behavioral characteristics as the input parameters are changed.

5.4.2.1 Applied Pressure Variation

Balloon expansion occurs only when the applied pressure in the mold is within a recommended range. If the pressure is too low a balloon may not form. Inversely, if the pressure it is set too high, the tubing may burst as it expands.

5.4.2.1.1 Quantitative Observations

Similarly to the 3 mm balloons, an increase in applied pressure leads to a thin-walled balloon with a higher rated burst pressure.

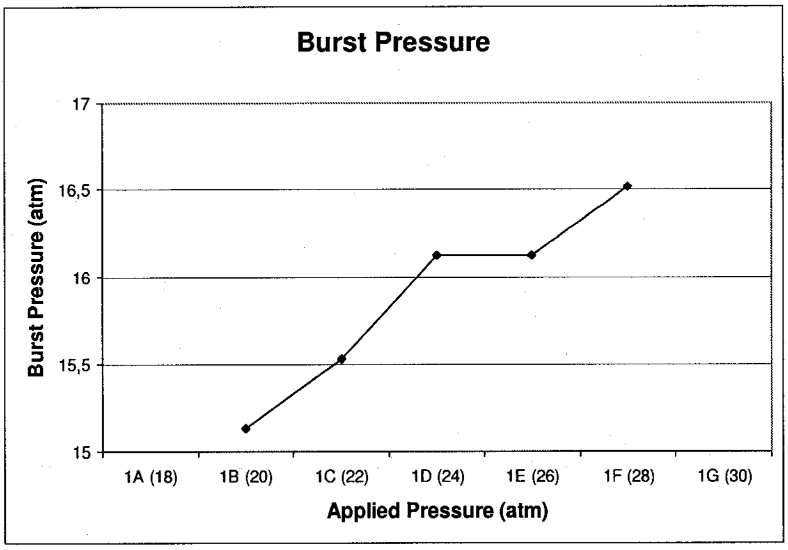


Figure 5-30 Burst Pressure as a Function of Applied Pressure

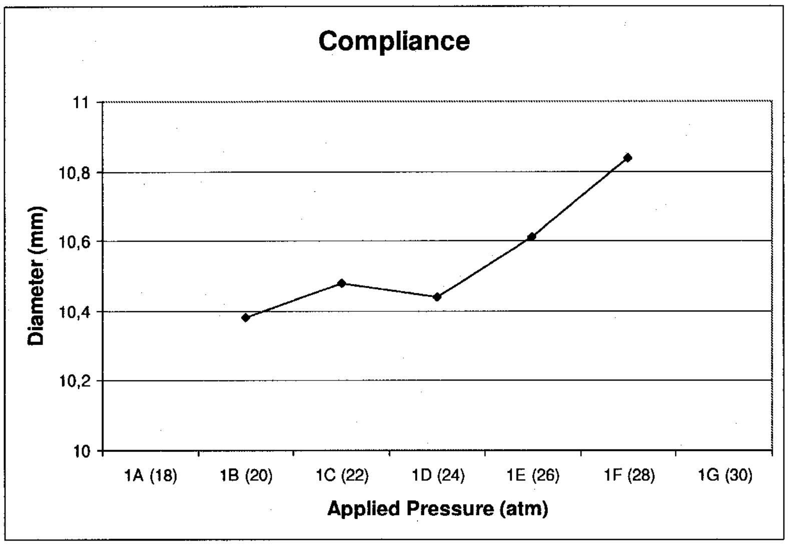


Figure 5-31 Compliance as a Function of Applied Pressure

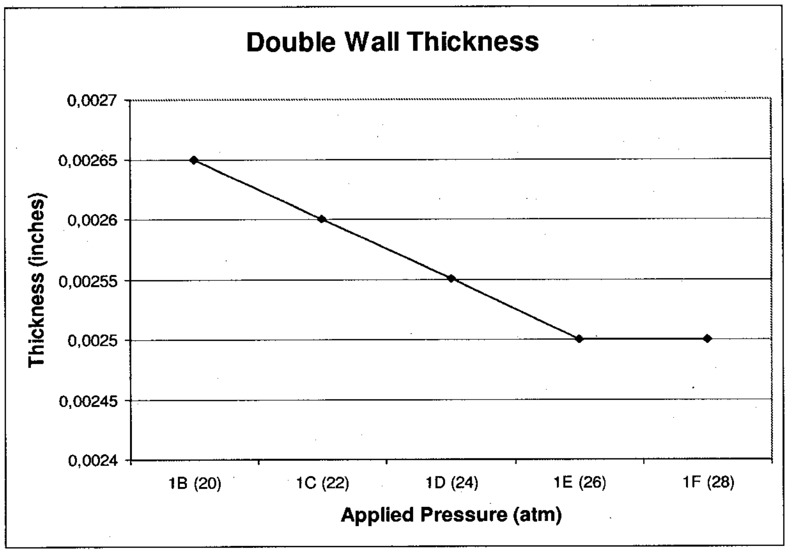


Figure 5-32 Wall Thickness as a Function of Applied Pressure

5.4.2.1.2 Qualitative Observations

A balloon free of defects and with nearly perfect material distribution is obtained when the applied pressure ranges between 22 and 26 atmospheres (2.23 to 2.63 MPa).

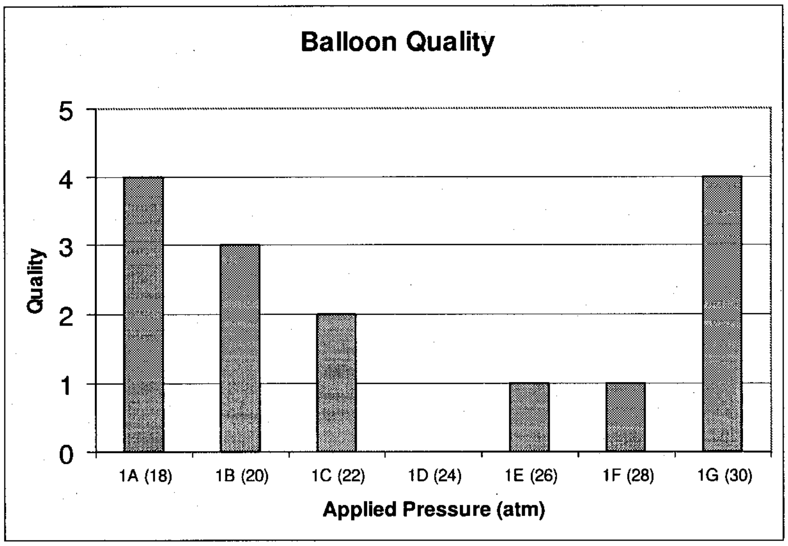


Figure 5-33 Balloon Quality as a Function of Applied Pressure

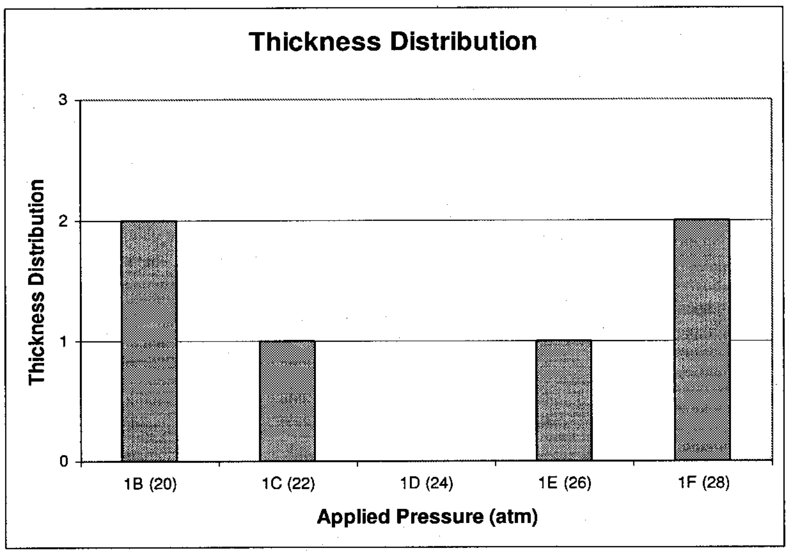


Figure 5-34 Material Distribution as a Function of Applied Pressure

5.4.2.2 Mold Temperature Variation

The mold temperature for 8 x 30 mm balloons ranges from 40 to 100°C (313 to 373 K). It is normally higher than for the smaller balloon because a larger material mass needs to be heated.

5.4.2.2.1 Quantitative Observations

These results follow the same pattern as for the 3 x 15 mm balloon. The rated burst pressure and compliance increase as the mold gets warmer. On the other hand, higher temperatures generally reduce wall thickness.

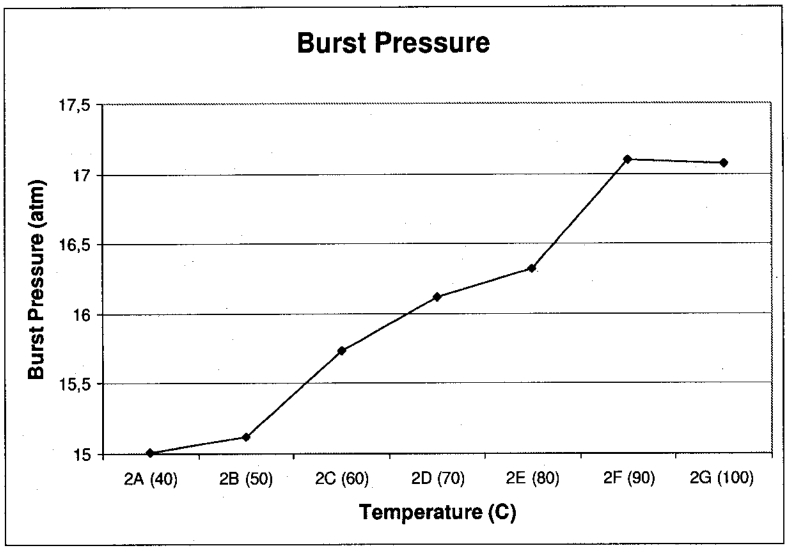


Figure 5-35 Burst Pressure as a Function of Mold Temperature

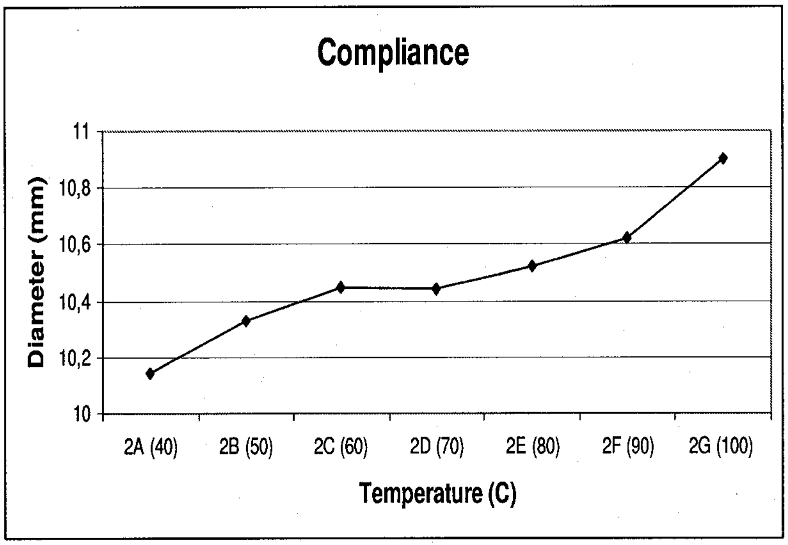


Figure 5-36 Compliance as a Function of Mold Temperature

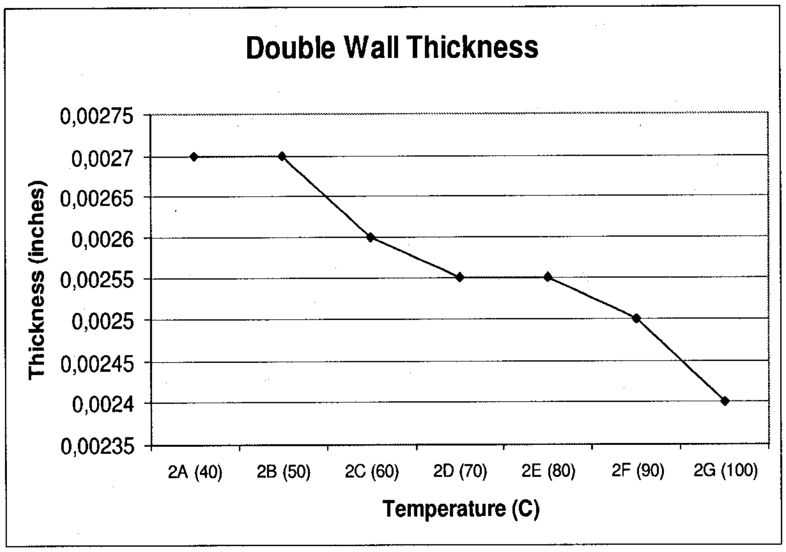


Figure 5-37 Wall Thickness as a Function of Mold Temperature

5.4.2.2.2 Qualitative Observations

Mold temperature, for best results, range from 50 to 80°C (323 to 353 K).

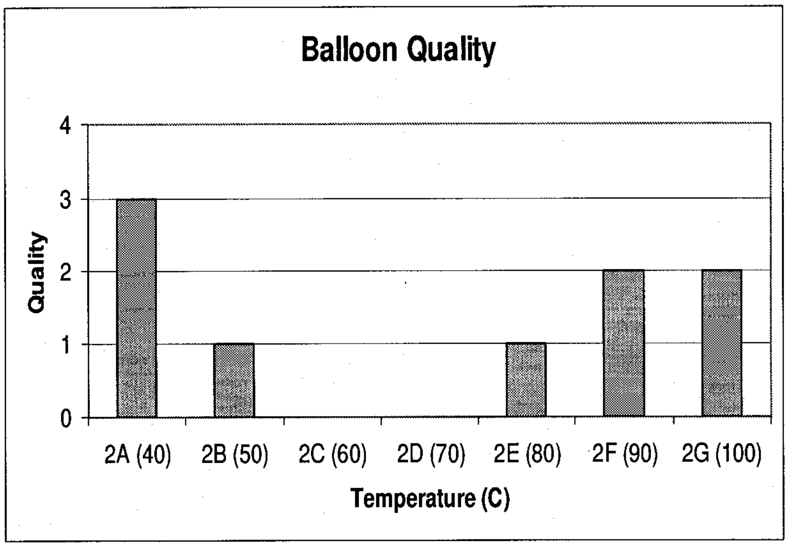


Figure 5-38 Balloon Quality as a Function of Mold Temperature

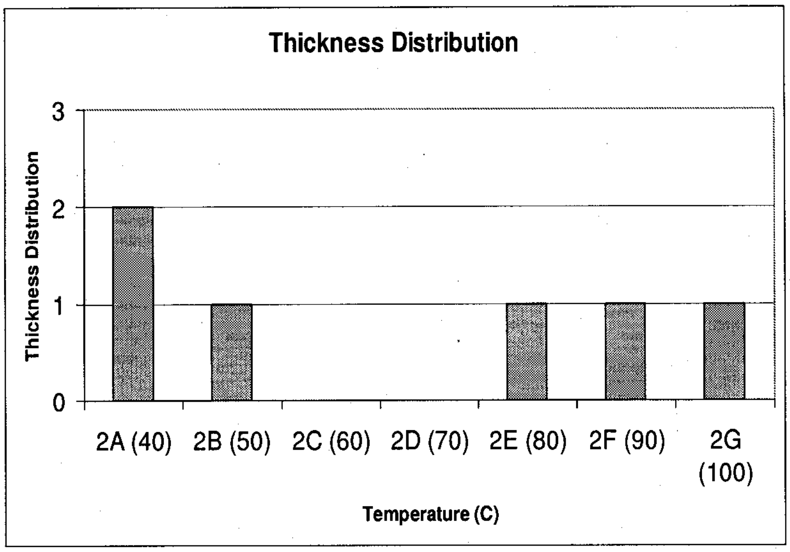


Figure 5-39 Material Distribution as a Function of Mold Temperature

5.4.2.3 Heat Time Variation

The heat time is typically longer for the larger balloon, since as previously noted, the mass to be heated is larger. For this trial, the range of time is between 110 to 170 seconds.

5.4.2.3.1 Quantitative Observations

In a pattern akin to that of the smaller balloon, the rated burst pressure, compliance, and wall thickness all tend to decrease as the heat time increases to 170 seconds.

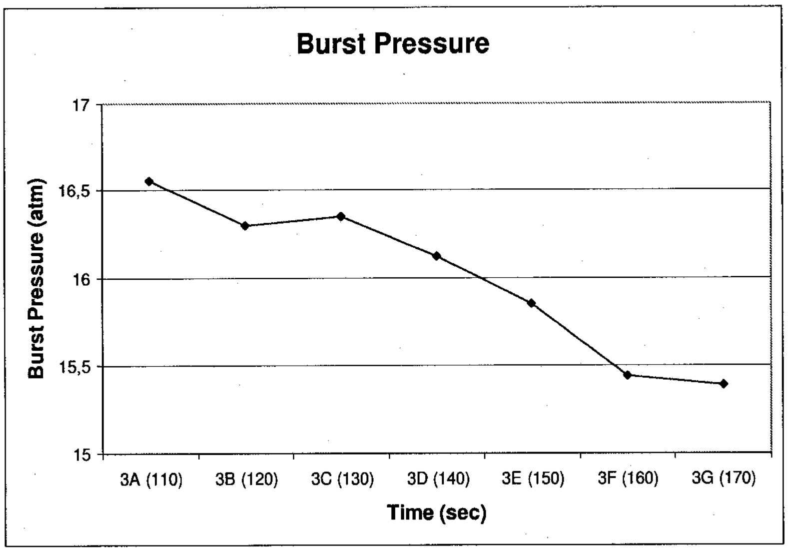


Figure 5-40 Burst Pressure as a Function of Heat Time

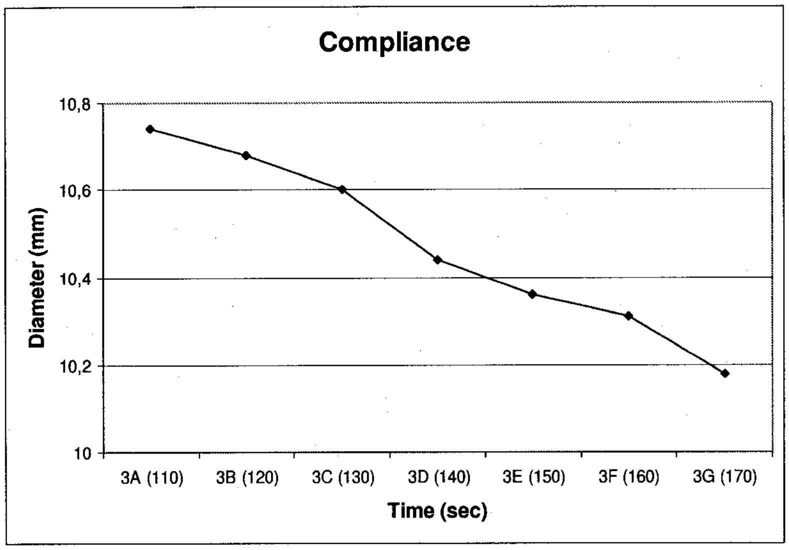


Figure 5-41 Compliance as a Function of Heat Time

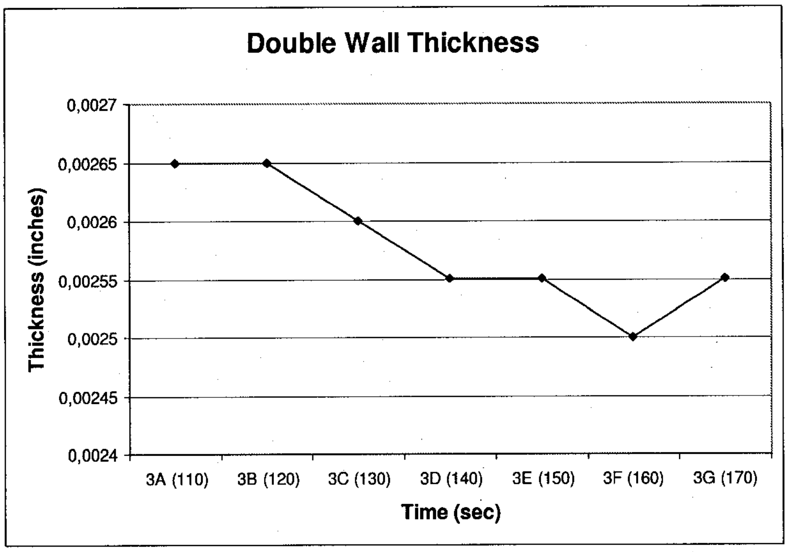


Figure 5-42 Wall Thickness as a Function of Heat Time

5.4.2.3.2 Qualitative Observations

Figure 5-43 shows that when the heat time is between 130 and 150 seconds balloon quality is optimized.

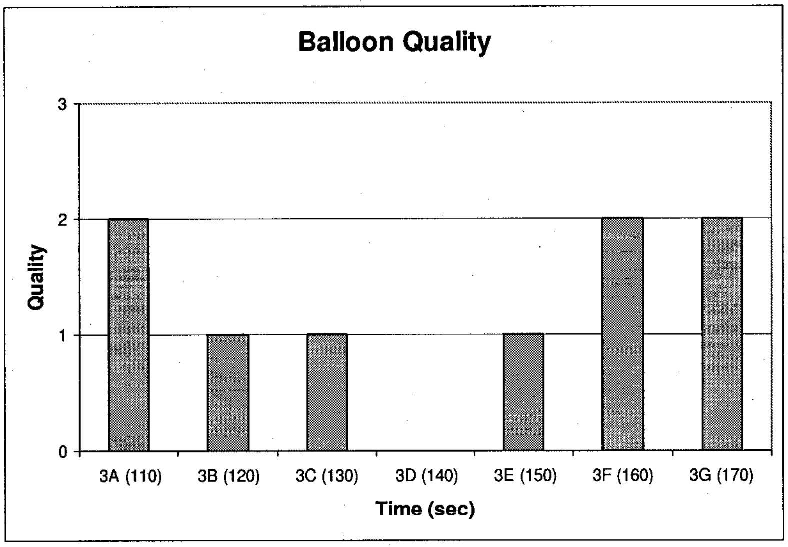


Figure 5-43 Balloon Quality as a Function of Heat Time

Figure 5-44 shows that when the heat time is between 130 and 150 seconds material thickness distribution is optimized.

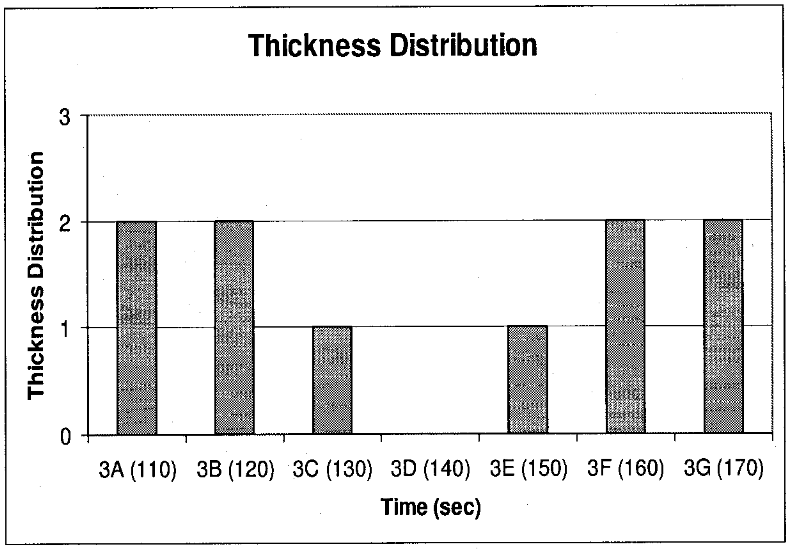


Figure 5-44 Material Distribution as a Function of Heat Time

5.4.2.4 Stretch Distance Variation

Larger balloons normally require longer stretch distances. For 8 mm angioplasty balloons a stretch ranging from 24 mm to 36 mm is typical.

5.4.2.4.1 Quantitative Observations

The graphs below illustrate that shorter stretch distances produce balloons with a higher rated burst pressure, as well as a higher balloon compliance and wall thickness.

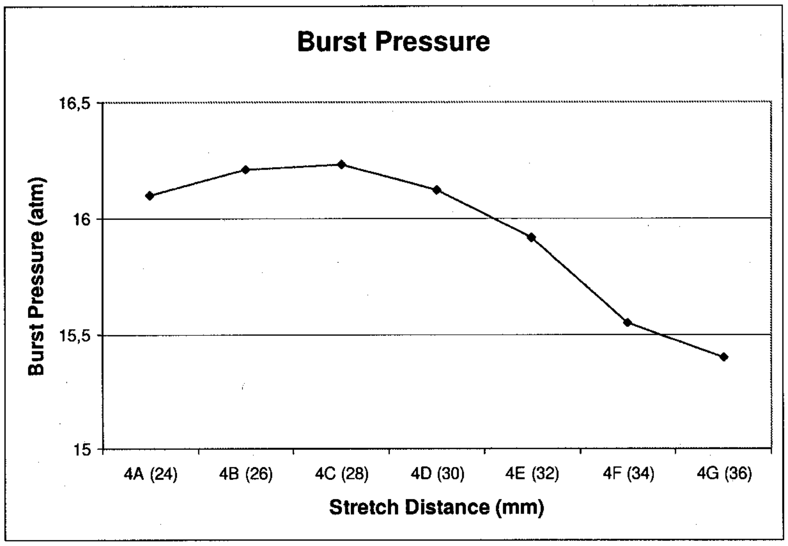


Figure 5-45 Burst Pressure as a Function of Stretch Distance

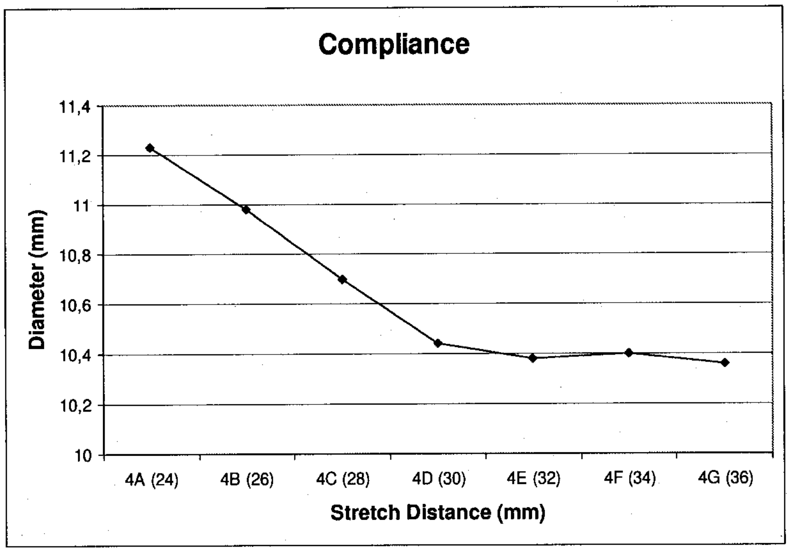


Figure 5-46 Compliance as a Function of Stretch Distance

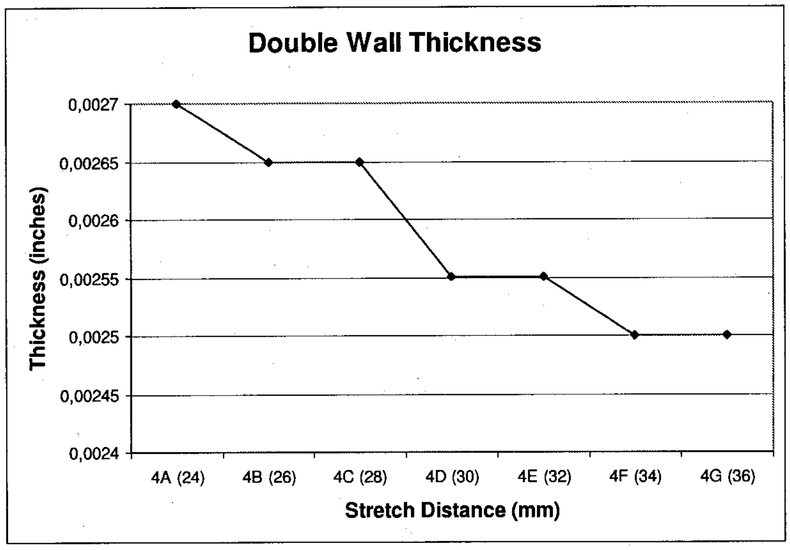


Figure 5-47 Wall Thickness as a Function of Stretch Distance

5.4.2.4.2 Qualitative Observations

Near perfect balloons are obtained when stretch distances range from 28 to 32 mm.

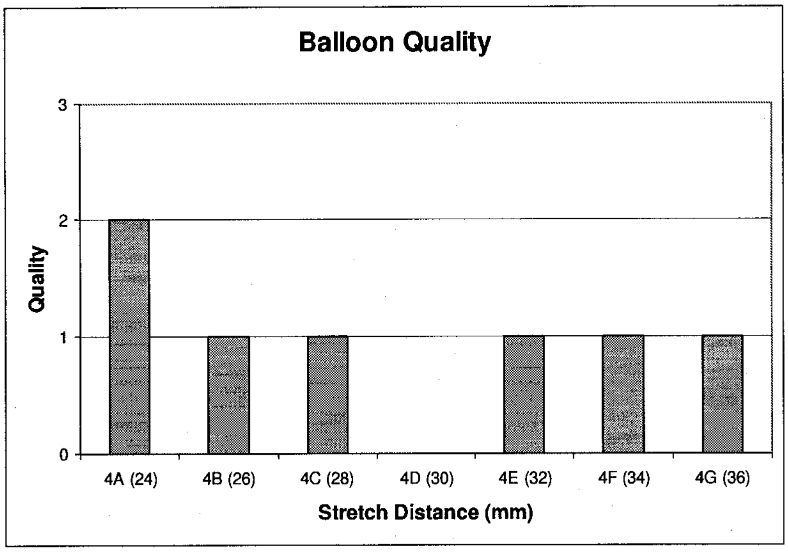


Figure 5-48 Balloon Quality as a Function of Stretch Distance

Material distribution is optimized when the stretch ranges from 28 to 34 mm.

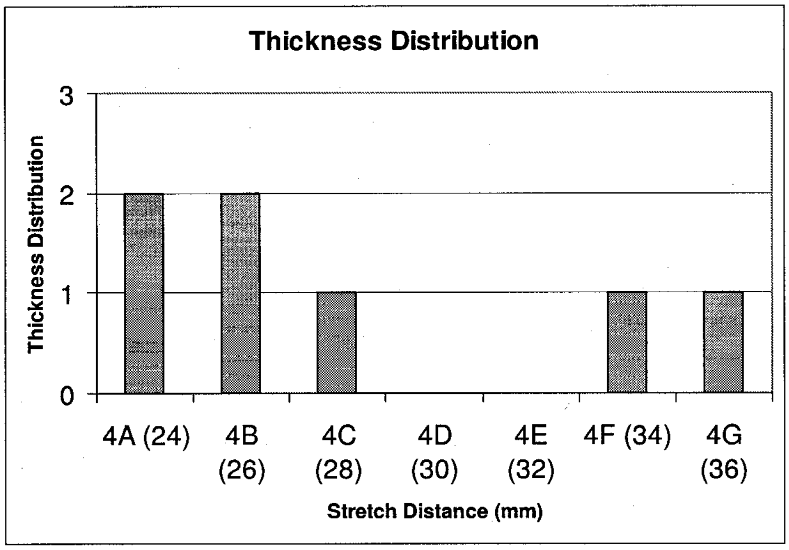


Figure 5-49 Material Distribution as a Function of Stretch Distance

5.4.2.5 Parison Length Variation

Since the 8 x 30 mm balloon is twice as long as the 3 x 15 mm balloon, the parison should be proportionally twice as long as well. For these larger balloons parison lengths from 19 to 31 mm are typical.

5.4.2.5.1 Quantitative Observations

The graphs below show that the rated burst pressure and balloon compliance are slightly higher as parison length increases to 31 mm. Wall thickness though decreases slightly as the parison length increases to 31 mm.

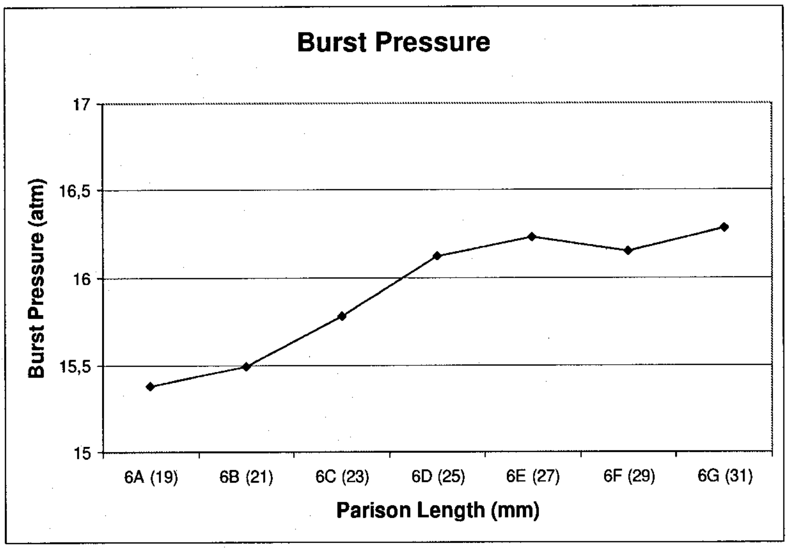


Figure 5-50 Burst Pressure as a Function of Parison Length

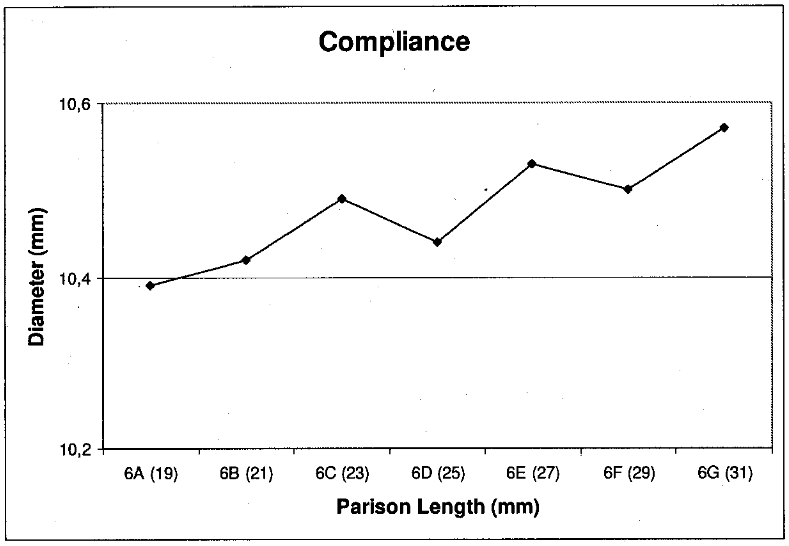


Figure 5-51 Compliance as a Function of Parison Length

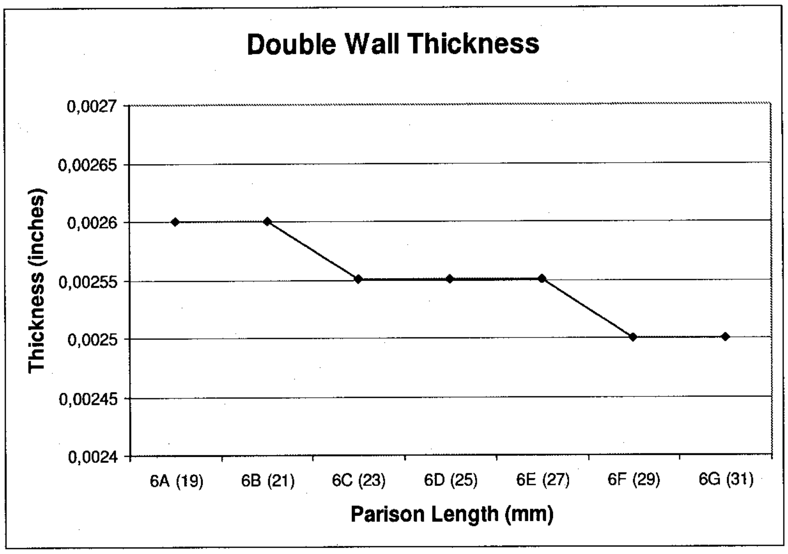


Figure 5-52 Wall Thickness as a Function of Parison Length

5.4.2.5.2 Qualitative Observations

A parison length between 21 and 27 mm will produce a higher quality balloon with a more constant material distribution.

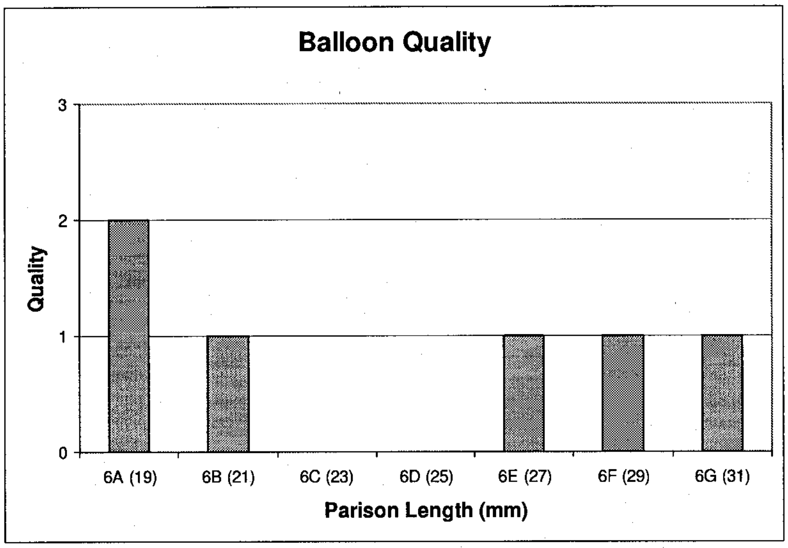


Figure 5-53 Balloon Quality as a Function of Parison Length

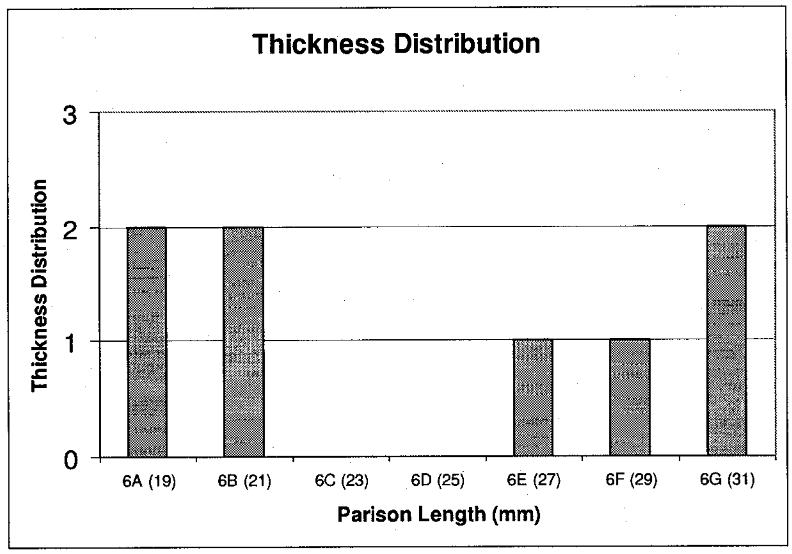


Figure 5-54 Material Distribution as a Function of Parison Length

The above data will now enable to generate a matrix that represents the model of relationships of the Balloon Forming Machine inputs and outputs.

5.5 Formulating the 'A' Matrix

The 'A' matrix is a Jacobian, or sensitivity, matrix relating the output parameters to the input parameters. It is a matrix where the value of each term can be viewed as the partial derivative of each of the three outputs to each of the five optimal inputs shown below.

$$A = \begin{bmatrix} \left.\frac{\partial P_{burst}}{\partial P_{app}}\right|_{P=35atm} & \left.\frac{\partial P_{burst}}{\partial T}\right|_{T=60} & \left.\frac{\partial P_{burst}}{\partial t}\right|_{t=60} & \left.\frac{\partial P_{burst}}{\partial d}\right|_{d=13.5} & \left.\frac{\partial P_{burst}}{\partial l}\right|_{l=15} \\ \left.\frac{\partial Thick}{\partial P_{app}}\right|_{P=35atm} & \left.\frac{\partial Thick}{\partial T}\right|_{T=60} & \left.\frac{\partial Thick}{\partial t}\right|_{t=60} & \left.\frac{\partial Thick}{\partial d}\right|_{d=13.5} & \left.\frac{\partial Thick}{\partial l}\right|_{l=15} \\ \left.\frac{\partial D_{\max}}{\partial P_{app}}\right|_{P=35atm} & \left.\frac{\partial D_{\max}}{\partial T}\right|_{T=60} & \left.\frac{\partial D_{\max}}{\partial t}\right|_{t=60} & \left.\frac{\partial D_{\max}}{\partial d}\right|_{d=13.5} & \left.\frac{\partial D_{\max}}{\partial l}\right|_{l=15} \end{bmatrix}$$

Equation 5-1 Jacobian Matrix used for 3 x 15 mm Balloons

The first term is basically the slope of the burst pressure at the applied pressure of 35 atmospheres (3.55 MPa), seen in Figure 5-3. The second term in the first row of the matrix is the rate of change of the burst pressure at an optimal mold temperature of 60°C (333 K) from Figure 5-10. Similarly, the second row is the slope of the double-wall thickness of a balloon with respect to each of the five optimal inputs. The last row is the slope of the maximum obtainable diameter in relation to all the optimal inputs.

5.5.1 Matrix 'A' for 3 x 15 mm Balloons

The matrix below is the 'A' matrix obtained from the 3 x 15 mm balloon tests.

$$A = \begin{bmatrix} -0.35 & 0.065 & -0.09 & -0.85 & 0.4 \\ -25e-6 & 0 & 0 & -25e-6 & 0 \\ -0.025 & 0.004 & -0.004 & -0.0035 & 0.01 \end{bmatrix}$$

Equation 5-2 Matrix 'A' for 3 x 15 mm Balloons

The second row with values all practically equal to zero is not desirable because it creates a matrix that is nearly not full rank. In order to allow this matrix to have a better condition number it may be pre-multiplied by a scaling matrix shown below. The modified 'A' matrix is in Equation 5-3.

$$A_1 A = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 10000 & 0 \\ 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} -0.35 & 0.065 & -0.09 & -0.85 & 0.4 \\ -25e-6 & 0 & 0 & -25e-6 & 0 \\ -25e-3 & 0.004 & -0.004 & -0.0035 & 0.01 \end{bmatrix}$$

$$A_{\text{mod}} = \begin{bmatrix} -0.35 & 0.065 & -0.09 & -0.85 & 0.4 \\ -0.25 & 0 & 0 & -0.25 & 0 \\ -0.025 & 0.004 & -0.004 & -0.0035 & 0.01 \end{bmatrix}$$

Equation 5-3 Modified Matrix 'A' for 3 x 15 mm Balloons

The scaling matrix allows for the new modified 'A' matrix to possess terms with similar magnitude. As a result, the units in the second row switch from inches to 1/10000 of an inch for the balloon's double-wall thickness.

5.5.2 Matrix 'A' for 8 x 30 mm Balloons

The same steps are taken to obtain the 'A' matrix for the larger balloons. The values found are shown below.

$$A = \begin{bmatrix} \frac{\partial P_{burst}}{\partial P_{app}}\Big|_{P=35atm} & \frac{\partial P_{burst}}{\partial T}\Big|_{T=60} & \frac{\partial P_{burst}}{\partial t}\Big|_{t=60} & \frac{\partial P_{burst}}{\partial d}\Big|_{d=13.5} & \frac{\partial P_{burst}}{\partial l}\Big|_{l=15} \\ \frac{\partial Thick}{\partial P_{app}}\Big|_{P=35atm} & \frac{\partial Thick}{\partial T}\Big|_{T=60} & \frac{\partial Thick}{\partial t}\Big|_{t=60} & \frac{\partial Thick}{\partial d}\Big|_{d=13.5} & \frac{\partial Thick}{\partial l}\Big|_{l=15} \\ \frac{\partial D_{\max}}{\partial P_{app}}\Big|_{P=35atm} & \frac{\partial D_{\max}}{\partial T}\Big|_{T=60} & \frac{\partial D_{\max}}{\partial t}\Big|_{t=60} & \frac{\partial D_{\max}}{\partial d}\Big|_{d=13.5} & \frac{\partial D_{\max}}{\partial l}\Big|_{l=15} \end{bmatrix}$$

$$A = \begin{bmatrix} 0.1475 & 0.0295 & -0.025 & -0.0775 & 0.1125 \\ -25e-6 & -2.5e-6 & -2.5e-6 & -25e-6 & 0 \\ 0.0325 & 0.0035 & -0.012 & -0.08 & 0.01 \end{bmatrix}$$

Equation 5-4 Matrix 'A' for 8 x 30 mm Balloons

Once again a scaling matrix is required to eliminate the second row with terms practically equal to zero. The modified matrix is found in Equation 5-5 where the units in the second row are once again changed to 1/10000 of an inch.

$$A_{\text{mod}} = \begin{bmatrix} 0.1475 & 0.0295 & -0.025 & -0.0775 & 0.1125 \\ -0.25 & -0.025 & -0.025 & -0.25 & 0 \\ 0.0325 & 0.0035 & -0.012 & -0.08 & 0.01 \end{bmatrix}$$

Equation 5-5 Modified Matrix 'A' for 8 x 30 mm Balloons

5.5.3 Considering Noise

In an ideal world these 'A' matrices obtained would be perfect to use in the ILC algorithms for the 3 mm and 8 mm balloons. Unfortunately the Balloon Forming Machine, along with all other machines, contains noise or perturbations during the molding of an angioplasty balloon. Furthermore, the relationship between the input and output variables is nonlinear and material dependent. Therefore, to compensate for these perturbations, an error term has been included in the 'A' matrix. With the help of the *rand* function in MATLAB™, used to create random numbers, each term in the 'A' matrix is randomly varied by +/-10 percent to simulate noise factor. It is this modified matrix that is used in the tests of the ILC algorithm. As a result each simulation of the ILC algorithm will produce a different 'A' matrix which is more realistic. The *rand* function can be found in the Matlab files in Appendix C.

Now that a model has been derived the next step is to implement a cycle-to-cycle controller from Iterative Learning Control theory.

6 CYCLE-TO-CYCLE CONTROLLER ON BFM

No specifically dedicated controller has yet been devised to improve and accelerate the manufacturing process of medical balloons. The rate at which balloons are produced depends mainly on the trial-and-error experience of the person running the Balloon Forming Machine. Although operator experience is a valuable asset it cannot match the productivity, reliability, and consistency of a BFM equipped with a controller.

The information in this document aims to reduce the time, material and energy spent on the production of medically acceptable angioplasty balloons. With the data gathered from the tests described in the previous chapter, it is possible to design a cycle-to-cycle controller capable of predicting a sensible starting point in terms of input selection. The control theory used to design this CTC controller is called Iterative Learning Control.

6.1 System Identification

The first step to designing a CTC controller is the identification of the system in use. The last chapter outlined the five selected inputs: *applied pressure* P (atm), *mold temperature* T (°C), *heat time* t (sec), *stretch distance* d (mm), and *parison length* l (mm). It also identified the measurable outputs: *burst pressure* P_{burst} (atm), *double-wall thickness* $Thickness_{DW}$ (inches), and *maximum diameter* D_{max} (mm) attained before burst. These parameters are defined as follows in MATLAB™, a software program used to run the ILC algorithm.

$$u = \begin{bmatrix} P \\ T \\ t \\ d \\ l \end{bmatrix}$$

Equation 6-1 Selected Input Parameters

$$y = \begin{bmatrix} P_{burst} \\ Thickness_{DW} \\ D_{\max} \end{bmatrix}$$

Equation 6-2 Selected Output Parameters

The parameter values used to obtain optimal performance angioplasty balloons are indicated by an asterisk. The optimal inputs used for the 3mm and 8mm angioplasty balloons, shown in Equation 6-3, are those that are likely to produce balloons with the best performance results.

$$u^* = \begin{bmatrix} P^* \\ T^* \\ t^* \\ d^* \\ l^* \end{bmatrix} = \begin{bmatrix} 35 \\ 60 \\ 60 \\ 13.5 \\ 15 \end{bmatrix}_{3mm} = \begin{bmatrix} 24 \\ 70 \\ 140 \\ 30 \\ 25 \end{bmatrix}_{8mm}$$

Equation 6-3 Optimal Input Parameters

These input parameters produce balloons with the optimal output values shown in Equation 4. These values imply that a 3 x 15 mm optimal balloon, having a double-wall thickness of 15/10000 of an inch (0.0381mm), should burst at approximately 23 atmospheres (2.33 MPa) while attaining a diameter of 3.84 mm before rupturing.

$$y^* = \begin{bmatrix} P^*_{burst} \\ Thickness^*_{DW} \\ D^*_{\max} \end{bmatrix} = \begin{bmatrix} 23.2 \\ 0.0015 \\ 3.84 \end{bmatrix}_{3mm} = \begin{bmatrix} 16.12 \\ 0.00255 \\ 10.44 \end{bmatrix}_{8mm}$$

Equation 6-4 Optimal Output Parameters

These results, along with the 'A' matrix from the previous chapter, make it possible to predict the change Δy in output y for any change Δu in input u. It should be noted that the 'A' matrix is only used within the linear range *about* the operating points. Any values which are more remote from the operating points will not be correctly predicted. This relation is found in Equation 6-5.

$$\Delta y = A\Delta u$$

Equation 6-5 Input/Output Relation

Equation 5 can be expanded. By definition,

$$\Delta u = u - u^*$$
and
$$\Delta y = y - y^*$$

Equation 6-6 Difference in Input and Output

Plugging Equation 6-6 into Equation 6-5 gives:

$$y - y^* = A(u - u^*)$$

Equation 6-7 Modified Input/Output Relation

Finally, by isolating for *y*, the most important equation used to predict the system output is derived.

$$y = A(u - u^*) + y^*$$

Equation 6-8 Predicting the Output for a given Input

This last equation states that given the optimal input u^*, output y^*, and the 'A' matrix, it is possible to find an output y for a selected input u. Equation 6-8 is used to test the validity of the 'A' matrix used in the ILC algorithm. This validity assessment process is explained in more detail in the next chapter. A validated matrix will allow the algorithm to make accurate predictions.

6.2 Introduction to Iterative Learning Control

Iterative Learning Control, or ILC, is a methodology for reducing errors from trial-to-trial for systems that operate repetitively [21]. The Balloon Forming Machine is such a system. ILC theory can be used to improve system response. The methodology is based on the premise that, if a system is run with operating parameters unchanged, the outputs will also remain unchanged, or alternatively, the errors observed will also remain unchanged no matter how often the tests are repeated. ILC methodology requires that errors in each iteration be recorded and it should help compute the modifications to the inputs to be applied to the next iteration. The goal is a progressive reduction of the error in the next iterative output until the error term disappears entirely.

6.2.1 Types of Linear ILC Algorithms

6.2.1.1 P-Type ILC

There are many types of linear ILC algorithms. Most existing ILC algorithms are either P-type or D-type or a combination of both [28]. The first and most basic algorithm is the proportional or P-type ILC shown in Equation 6-9.

$$u_{k+1}(t) = u_k(t) + \gamma e_k(t)$$

Equation 6-9 P-Type ILC Algorithm

The P-type ILC predicts the next input by adding the product of the system output errors and a constant learning gain γ to the current input $u_k(t)$. It is the "terminal" version of this algorithm (TILC) that is applied in this thesis work. That is the inputs are assumed constant throughout the cycle, and, only at the end of the cycle is the output measured to form a constant error vector. Note that in this case Equation 6-9 yields an integral-type TILC, where the term integral refers to the cycle-to-cycle accumulation of the error.

6.2.1.2 D-Type ILC

The second type is the D-type or derivative-type ILC. This algorithm is very similar to the P-type except that the D-type ILC utilizes the derivatives of the system output errors. Equation 6-10 represents the D-type algorithm.

$$u_{k+1}(t) = u_k(t) + \gamma \frac{d}{dt} e_k(t) = u_k(t) + \gamma \frac{(e_k(t+1) - e_k(t))}{T}$$

Equation 6-10 D-Type ILC Algorithm

One advantage of the D-type ILC is that it guarantees exponential convergence of the error signals with respect to the number of iterations at the cost of the measurements of the system output derivatives[28].

6.2.1.3 PD-Type ILC

When P-type and D-type ILC algorithms are combined, the resulting algorithm is called a proportional-derivative or PD-type ILC. This algorithm has shown to be effective in ensuring the convergence of the tracking errors [28]. The PD-type ILC is seen in the equation below.

$$u_{k+1}(t) = u_k(t) + \gamma_1 e_k(t) + \gamma_2 \frac{d}{dt} e_k(t)$$

Equation 6-11 PD-Type ILC

6.2.1.4 PID-Type ILC

The PID-type ILC algorithm is simply the combination of the proportional, integral, and derivative tracking errors seen underneath.

$$u_{k+1}(t) = u_k(t) + \gamma_1 e_k(t) + \gamma_2 \int_0^t e_k(\tau) d\tau + \gamma_3 \frac{d}{dt} e_k(t)$$

Equation 6-12 PID-Type ILC

In recent years other versions of ILC algorithms have been derived and used in all sorts of applications. ILC can be applied to open-loop or closed-loop systems, discrete-time or continuous-time systems, linear or nonlinear systems, time-invariant or time-varying systems, and other systems. Section 6.2.2 lists a few of the many applications that ILC methodology has helped improve.

6.2.2 ILC Applications

Over recent years the Iterative Learning Control methodology has had an astounding impact on the performance of controllable systems. ILC has helped these systems become more efficient by introducing progressive improvement following each iterative cycle. Take, for example, a robotic arm that pours molten metal into a mold. Normally the robot arm waits in its home position until the mold closes after a part is removed. The closed mold triggers the arm to dip a ladle into the pot, pick up a quantity of metal, and pour it into the mold. When the ladle is empty it returns to its home position until the mold is in ready mode to cast the next part.

A manufacturing robot that performs a given set of movements over and over again in an assembly line is only one of many applications that can be improved through ILC techniques. Electrical systems such as electrical drives, chemical process systems such as batch reactors, aerodynamic systems have also vastly improved system response from trial-to-trial, thanks in part to ILC [22].

6.2.3 Comparison of ILC to Other Control Paradigms

Iterative Learning Control is a control method that works best on systems that operate repetitively. Unlike most other control techniques such as feedback control, adaptive control, robust control, intelligent control, and optimal control, ILC permits progressively improved performance based on previous input signals and tracking errors, with less knowledge of the plant. For instance, a robotic manipulator uses the same repetitive trajectory to pick up a door panel, make a few welds, and put it back in place. If the robotic manipulator functions with only a feedback controller, the same tracking error would reappear within every execution. The replacement of the feedback controller with a learning controller improves the tracking performance with each progressive trial by using the information from the previous trial. As the number of executions increases the tracking error will tend to converge towards zero.

There are applications where some very simple repetitive cycles do not require any degree of learning. Most could use ILC learning to improve response, and for some applications, ILC methodology can have a major impact on system efficiency and overall response [30]. In addition, even with an inaccurate system model, it still may be possible for ILC to achieve optimal tracking performance [31]. As stated previously, the ILC algorithm elaborated in this document is the P-type ILC, or equivalently the integral TILC [32].

6.3 P-Type ILC Theory

A simple flow chart of Iterative Learning Control is illustrated in Figure 6-1 [22].

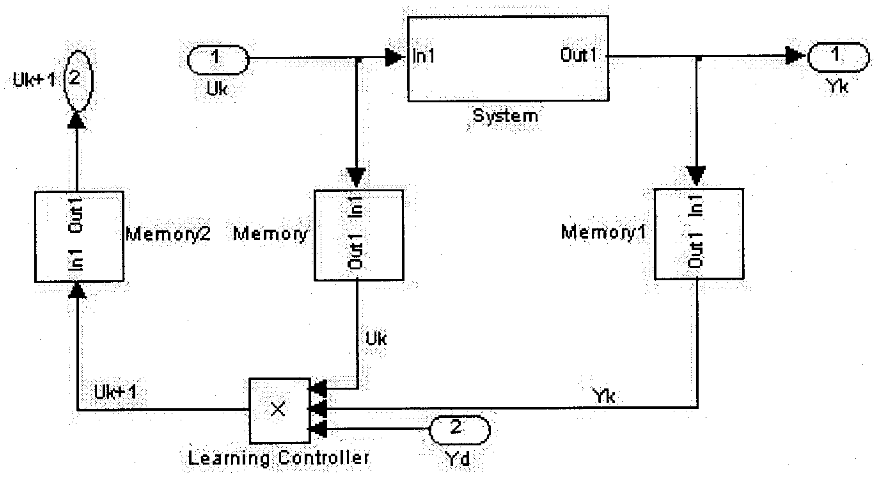


Figure 6-1 Iterative Learning Control Configuration

The subscript k represents the trial or iteration number in progress. The idea as to how Iterative Learning Control theory works is as follows: In the k^{th} trial an input $u_k(t)$ is entered into a system which in turn generates an output $y_k(t)$. These values are stored in memory until the results from the next trial are generated. From the error term, which is the difference between the desired and actual outputs, the ILC algorithm computes a new input signal $u_{k+1}(t)$ that will be inputted into the system [21]. This system will likely return an output with a smaller variance or error term than the previous trial. The iterative process is repeated until the error term converges towards zero and outputs a value acceptably close to the desired output. The P-type ILC algorithm can be represented by the following equation [21]; where the time dependency can be dropped.

$$u_{k+1} = u_k + \gamma e_k$$

Equation 6-13 P-Type ILC Algorithm

This last equation states that the next input is given by the sum of the current input and the learning gain γ of the controller amplified by the error term e_k. The learning gain γ is equal to the weighting matrix K multiplied with the pseudo inverse of the 'A' matrix. In this case the weighting matrix is represented by an identity matrix with ones along its diagonal and zeros everywhere else. This is explained in more detail in the following section. Accordingly, the learning gain is determined by using Equation 6-14.

$$\gamma = KA^{-1} = A^{-1}$$

Equation 6-14 Learning Gain of ILC

The error term for the k^{th} iteration is the difference between desired and actual outputs as shown in the equation below.

$$e_k = y_d - y_k$$

Equation 6-15 Error Term

Theoretically, the output y_k is obtained by multiplying the 'A' matrix with the input vector u_k as shown in Equation 6-16. The desired output y_d is selected by the operator.

$$y_k = Au_k$$

Equation 6-16 Determination of the Desired Output

On the machine, the term y_k is the actual output obtained from each test on the balloons expanded at the CNRC-NRC IMI biomedical laboratory. The modified error term is then derived using Equation 6-17 found below.

$$e_k = y_d - Au_k$$

Equation 6-17 Modified Error Term

By inserting Equations 6-14 and 6-15 into Equation 6-13, the final ILC algorithm for finding the next input is obtained.

$$u_{k+1} = u_k + A^{-1}(y_d - y_k)$$

Equation 6-18 Final ILC Algorithm

This last equation states that the addition of the current input to the product of the pseudo-inverse of matrix 'A' and the error term can help predict an improved value for the next input. The ILC control is shown in Figure 6-2.

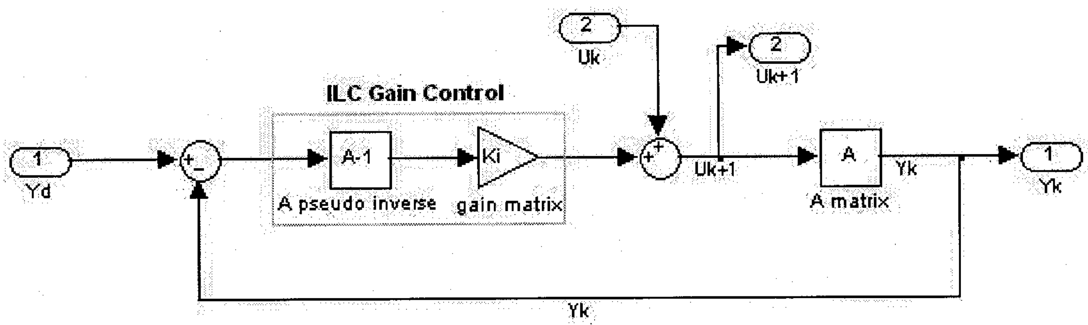


Figure 6-2 ILC Control Block Diagram

6.3.1 ILC Algorithm

The first step to the ILC algorithm is to enter an initial input u_0 into the Balloon Forming Machine. The initial output is y_0. The initial input and output values are then entered into the MATLAB™ program (found in Appendix C). The program then prompts the operator to enter the desired output y_d and runs the algorithm. When the calculations finish, the ILC algorithm recommends the next input u_1 to be entered into the BFM. The anticipated output y_1 should be closer to the desired output than the previous output y_0. The second generation of inputs and outputs are again entered into the program which then runs the ILC algorithm to compute the next recommended input u_2. The process continues until the output y_k is close enough to the desired output y_d.

6.3.1.1 Constraints

The constraints added in the ILC algorithm virtually eliminate the risk of producing balloons with physical defects such as crow feet and radial rings. The constraints also enhance the chances of expanding balloons with an even thickness distribution. From the experimental results obtained for the 3 x 15 mm balloons in Figure 5-7, a high quality balloon is obtained when the applied pressure lies between 33 and 39 atm. The thickness distribution, shown in Figure 5-9, is most uniform when the applied pressure stays within 31 and 39 atm. Hence the constraint used when varying the applied pressure to make a balloon with even wall thickness is simply the intersection of the two ranges as shown below:

$$(33 < P < 39) \cap (31 < P < 39) \Rightarrow 33 < P < 39$$

Equation 6-19 ILC Constraint for Applied Pressure of 3 x 15 Balloons

The constraints for the other input parameters are obtained in the same manner. Table 6-1 includes the constraints used for both the 3 mm and 8 mm ILC algorithms.

Input Parameters	3x15 mm Balloon Constraint	8x30 mm Balloon Constraint
Applied Pressure (atm)	33<P<39	22<P<26
Mold Temperature (°C)	55<T<65	50<T<80
Heat Time (sec)	50<t<65	130<t<150
Stretch Distance (mm)	12.5<d<15.5	28<d<32
Parison Length (mm)	13<l<18	21<l<27

Table 6-1 ILC Constraints for 3mm and 8mm Balloons

The addition of the constraints completes the ILC algorithm.

6.3.1.2 Example of ILC Algorithm

Assume that the BFM operator chooses an initial input equal to $u_0 = \begin{bmatrix} 33 \\ 65 \\ 55 \\ 13.5 \\ 15 \end{bmatrix}$, where the input parameters are respectively the *applied pressure* (atm), *mold temperature* (°C), *heat time* (sec), *stretch distance* (mm), and *parison length* (mm). When these values are entered, the Balloon Forming Machine produces a balloon with the characteristics $y_0 = \begin{bmatrix} 24.025 \\ 0.0016 \\ 3.93 \end{bmatrix}$, where the measurable outputs are *burst pressure* (atm), *double-wall thickness* (inches), and *maximum diameter* (mm) attained before burst.

The following step is to run the ILC algorithm where the program first prompts the user to enter the desired burst pressure:

Please enter the desired burst pressure within a desirable range (15-28 atm) or (1.5-2.8 MPa):
23.2 atm (2.32 MPa)

Next, it asks for the desired double-wall thickness:

Please enter the desired double-wall thickness within a desirable range (0.0012-0.0017") or (0.0305-0.0432 mm):
0.00135" (0.0343 mm)

Finally, the maximum diameter is requested:

Please enter the maximum desired diameter within a desirable range (3.3-4.7 mm):
3.84 mm

Once these values are entered, the algorithm computes the next input to be used on the Balloon Forming Machine:

The ILC recommends setting your next input to:

Applied Pressure (atm): 37.3 (3.78 MPa)
Mold Temperature (°C): 63.2 (336 K)
Heat Time (sec): 56.8
Stretch Distance (mm): 14
Parison Length (mm): 15

Thus, the next input set on the Balloon Forming Machine is $u_1 = \begin{bmatrix} 37 \\ 63 \\ 57 \\ 14 \\ 15 \end{bmatrix}$, since the machine only accepts integers. This input will then give the operator the values of y_1 from balloon testing which will in turn be entered into the algorithm to find u_2. These iterations continue until the output values measured in the laboratory are almost identical to the desired output values. It usually takes six to seven iterative cycles to reach this point.

7 Experimental Tests

Once the design of the cycle-to-cycle controller is completed, the experimental testing phase begins. This stage executes the many tests required to verify the validity of the ILC algorithms for 3 mm and 8 mm balloons. Before even testing the ILC algorithm however, it is important to first ascertain the validity of the 'A' matrices obtained. An invalid 'A' matrix yields erroneous input values for the Balloon Forming Machine. This in turn leads to the production of balloons having inferior performance characteristics.

7.1 Verification of 'A' Matrix

To validate the 'A' matrix Equation 6-8 is required. For a given input, this equation predicts the theoretical output results from balloon testing. Using identical input parameters, the necessary tests are performed on an actual angioplasty balloon. For the 'A' matrix to be valid, the theoretical and practical experimental values should be similar. The tests done on both sizes of balloons are detailed in the next pages.

7.1.1 Verification of the 'A' Matrix for 3 x 15 mm Balloons

Only three of the many tests conducted for 3 x 15 mm balloons are shown in Table 7-1 since they all lead to similar results.

	Inputs	Optimal Point		Results Obtained	Desired Results	Error %
Applied Pressure	33	35	Burst Pressure	22,16	24,025	7,762747
Temperature	55	60	Thickness	14,5	15	3,333333
Heat Time	55	60	Max Diameter	3,97	3,89	-2,05656
Stretch Distance	13,5	13,5				
Unstretched Length	15	15				
	Inputs	Optimal Point		Results Obtained	Desired Results	Error %
Applied Pressure	37	35	Burst Pressure	20,12	22,375	10,07821
Temperature	65	60	Thickness	15	15	0
Heat Time	65	60	Max Diameter	3,97	3,79	-4,74934
Stretch Distance	13,5	13,5				
Unstretched Length	15	15				
	Inputs	Optimal Point		Results Obtained	Desired Results	Error %
Applied Pressure	33	35	Burst Pressure	23,59	24,675	4,397163
Temperature	65	60	Thickness	15	15,5	3,225806
Heat Time	55	60	Max Diameter	4,04	3,93	-2,79898
Stretch Distance	13,5	13,5				
Unstretched Length	15	15				

Table 7-1 Verification of 'A' Matrix for 3 x 15 mm Balloons

The inputs shaded in dark grey are inputs that vary from the operating inputs but still lie within the linear range of the relationship. The 'A' matrix is based on the relation of the inputs to the output *about* the operating points. Thus, if the inputs were to be changed to values far from the operating points, the prediction of the outputs would be completely wrong.

As expected the theoretical results predicted are invariably within ten percent of the experimental results obtained in the laboratory. The first row under "results" is the burst pressure (atm), followed by double-wall thickness (1/10000"), and finally by the maximum diameter (mm). This 'A' matrix is valid for the ILC algorithm since it can reasonably predict the output for a given input.

7.1.2 Verification of the 'A' Matrix for 8 x 30 mm Balloons

Similar tests are also done for the larger balloons. Table 7-2 includes a few trials.

	Inputs	Optimal Point		Experimental Results	Theoretical Results	Error %
Applied Pressure	28	24	Burst Pressure	16,32	16,75	2,567164
Temperature	60	70	Thickness	25	23,5	-6,38298
Heat Time	150	140	Max Diameter	11,1	10,26	-8,18713
Stretch Distance	30	30				
Unstretched Length	25	25				
	Inputs	Optimal Point		Experimental Results	Theoretical Results	Error %
Applied Pressure	22	24	Burst Pressure	15,82	16,22	2,466091
Temperature	70	70	Thickness	25	24	-4,16667
Heat Time	150	140	Max Diameter	10,97	10,77	-1,85701
Stretch Distance	26	30				
Unstretched Length	25	25				
	Inputs	Optimal Point		Experimental Results	Theoretical Results	Error %
Applied Pressure	26	24	Burst Pressure	16,11	16,78	3,992849
Temperature	70	70	Thickness	24	23	-4,34783
Heat Time	130	140	Max Diameter	10,73	11,23	4,45236
Stretch Distance	34	30				
Unstretched Length	25	25				

Table 7-2 Verification of 'A' Matrix for 8 x 30 mm Balloons

Once again, since the predicted results are quite close to the actual experimental values, the 'A' matrix can be confirmed as being valid. The next step is to see if the ILC algorithm functions properly.

7.2 Verification of ILC Algorithm

A total of twenty angioplasty balloons are produced for this validation set. Ten balloons are formed using a tradition trial-and-error method based strictly on operator experience. The remaining ten balloons are produced using the ILC algorithm. These tests are applied to both the 3 mm and 8 mm angioplasty balloons.

7.2.1 Verification of ILC Algorithm for 3 x 15 mm Balloons

For this experiment the desired burst pressure is set at 23.50 atmospheres (2.38 MPa), the double-wall thickness at 0.0014 inches (0.0356 mm), and the maximum diameter at 3.80 mm. The graph below portrays the results obtained for the trials done with and without the controller.

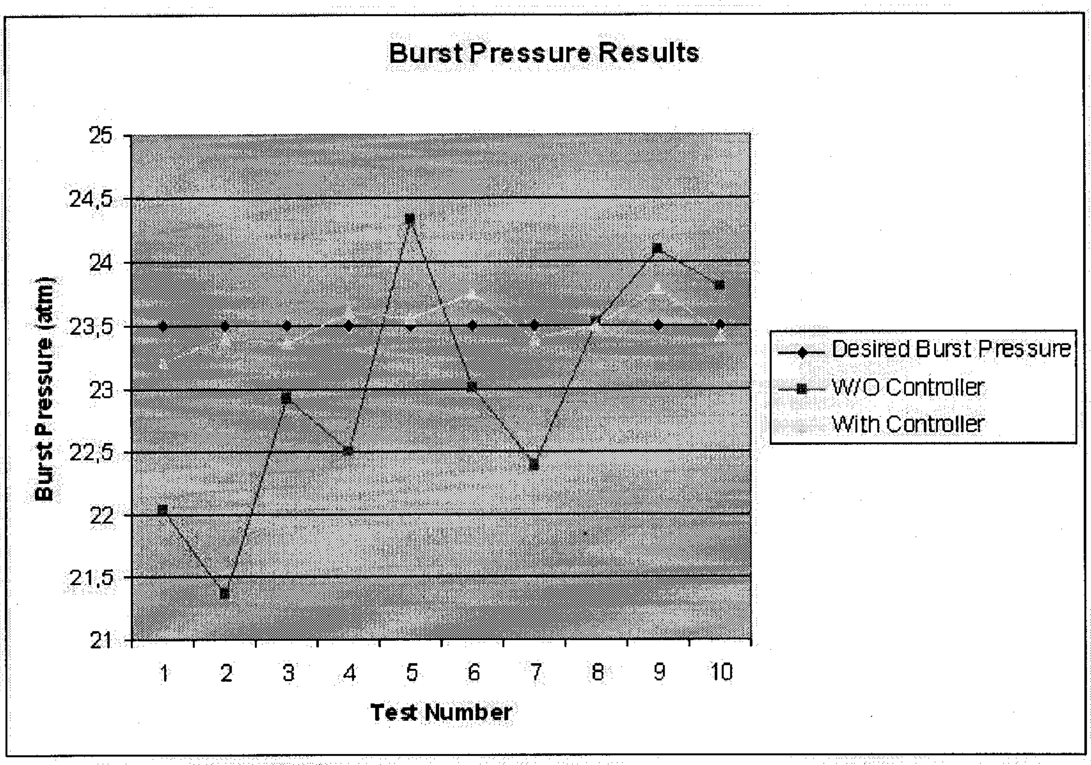


Figure 7-1 Burst Pressure Results with and without Controller

The ILC algorithm clearly reaches near the desired value at the initial trial and tends to remain closer when compared to the method using estimated trial-and-error. The problem with the traditional method is that a minor change in input may frequently cause a significant change in output. In test number four, without the controller, an operator would most likely decide to increase the applied pressure into the balloon to compensate for the low burst pressure value. However, a small increase in the applied pressure from 35 to 37 atmospheres (3.55 to 3.75 MPa), causes a burst pressure higher by almost two atmospheres, from 22.5 to 24.33 atm (2.28 to 2.47 MPa). The result from test five is too high and the operator has no choice but to lower the applied pressure or change another input parameter in an attempt to bring the burst pressure in line again.

The second output parameter analyzed is the double-wall thickness. Once again, according to Figure 7-2, convergence towards the desired values is faster and better with the controller than without.

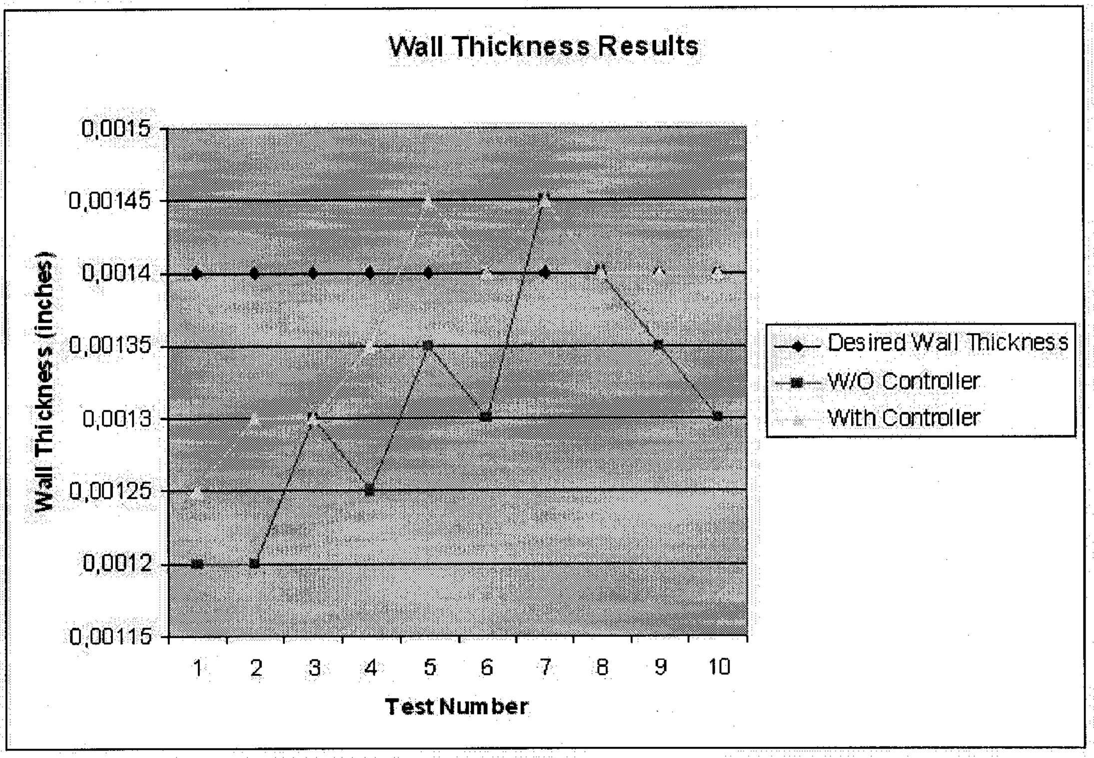


Figure 7-2 Double Wall Thickness Results with and without Controller

Although the values without the controller do tend to move towards the desired wall thickness, it does take more trials to attain it than when applying the ILC algorithm. The randomness of the trial-and-error method is evident in trials nine and ten where the resulting wall thickness actually diverges from the desired value.

The final parameter to compare is the balloon's maximum diameter before burst. In the figure below it is apparent that the controller does not maintain convergence as well as it did in the previous two figures.

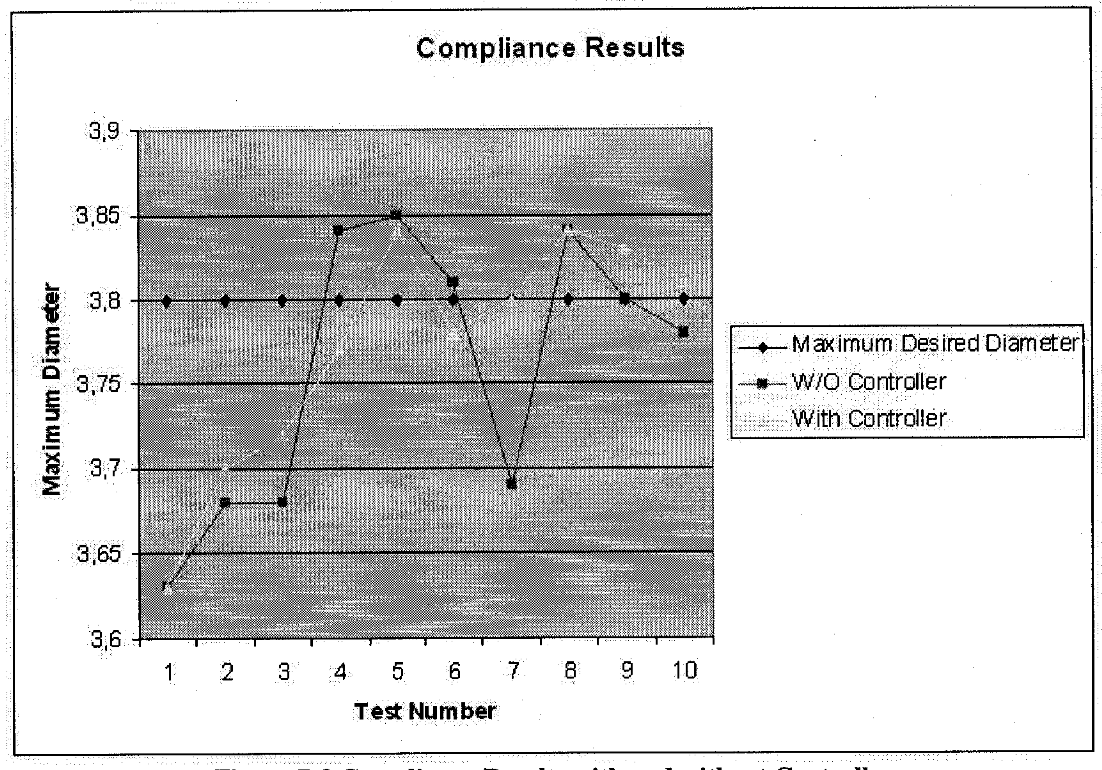


Figure 7-3 Compliance Results with and without Controller

This does make sense since it is practically impossible to form balloons that expand to the exact same diameter before bursting. Still, it should be noted that nevertheless, approximate convergence is attained faster than by the traditional method because it allows the operator to begin at a sensible starting point with less guess work as to what inputs to enter.

7.2.2 Verification of ILC Algorithm for 8 x 30 mm Balloons

The same process is used for the larger balloons to check the validity of the ILC algorithm. Ten balloons are produced with the cycle-to-cycle controller and ten are produced without it. Figure 7-4 below shows the results of the burst pressure for the 8 x 30 mm balloons. Although the values in yellow (with controller) obtained by using the algorithm do not converge precisely to the desired pressure of 16.5 atmospheres (1.67 MPa), it reduces significantly the variances obtained with the traditional trial-and-error method shown in pink. The fact that the results in yellow (with controller) alternate about the desired burst pressure indicates that the ILC algorithm is functioning correctly.

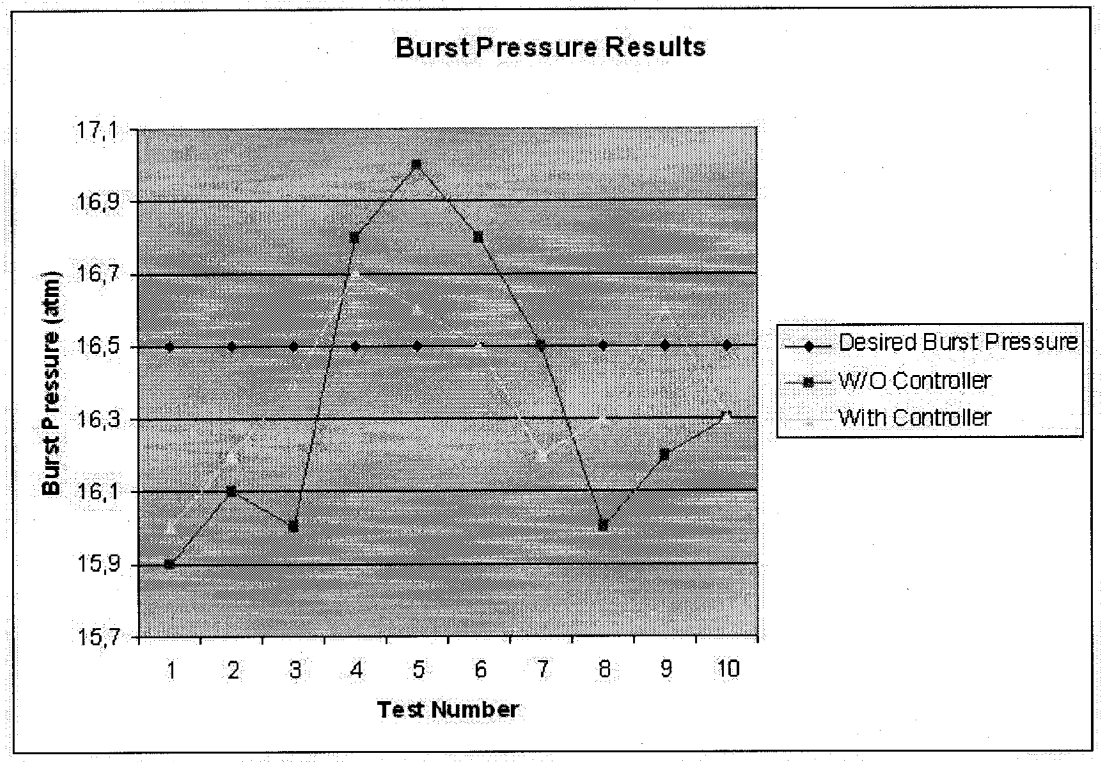


Figure 7-4 Burst Pressure Results with and without Controller

Similar to the burst pressure results balloons produced with the CTC controller do not converge precisely to the set thickness of 0.0024" (0.061 mm) as seen in Figure 7-5. These small divergences are normal since many other factors such as the force applied during stretching and the stretch speed are not taken into account. When the values remain *close* to the desired value, the ILC algorithm is considered valid. It is important to note that no two balloons will produce identical results even with identical inputs. The expectation to match the desired value at every trial is not realistic.

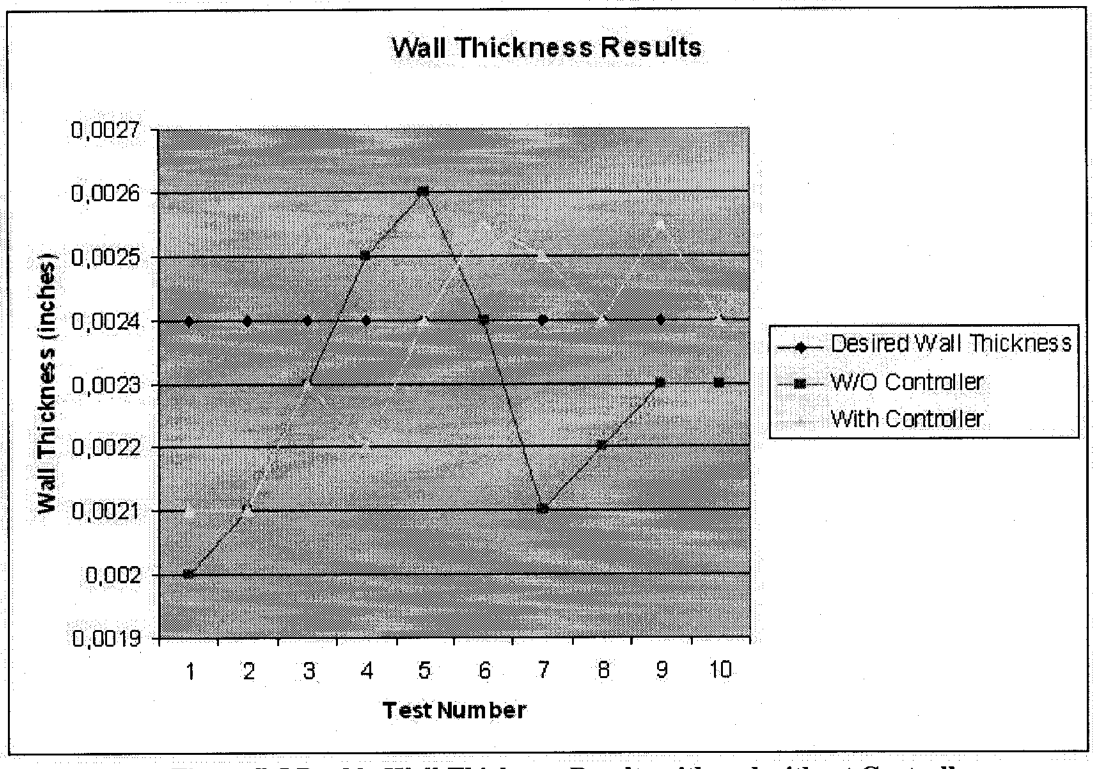


Figure 7-5 Double Wall Thickness Results with and without Controller

The following graph shows a comparison of the balloon compliance results with and without a controller. The ILC algorithm in this case works very well since there is a large discrepancy between the results obtained from balloons made with the CTC controller and those made without the controller.

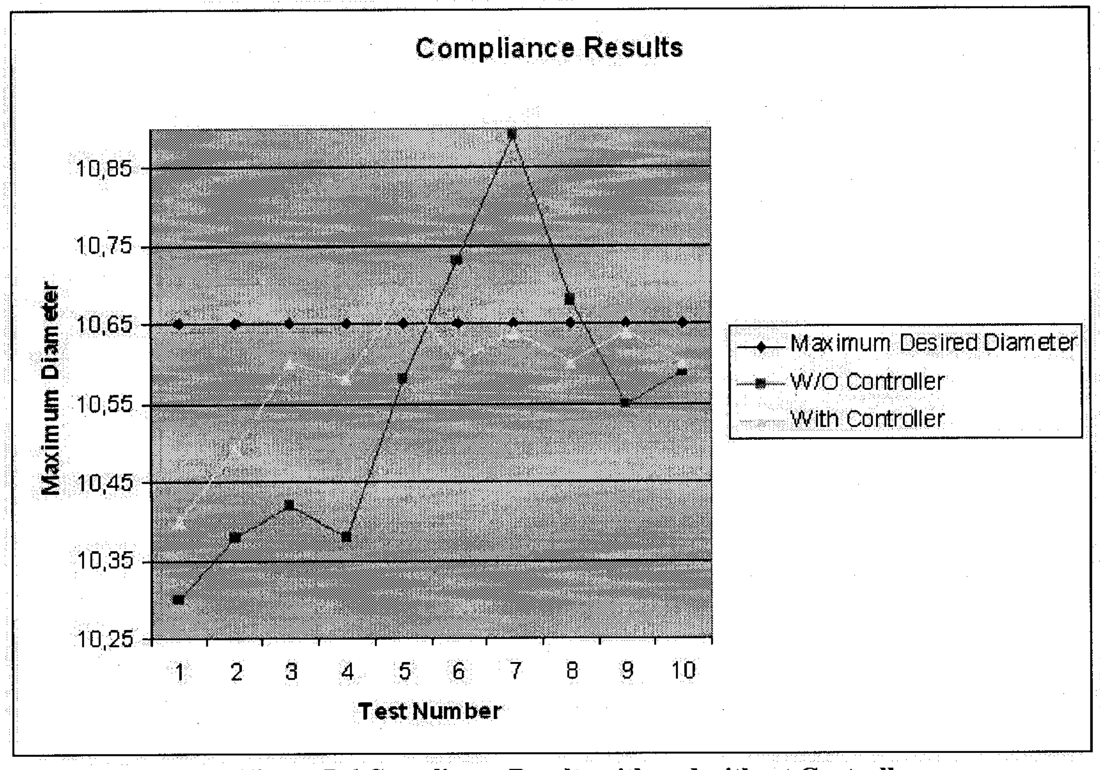


Figure 7-6 Compliance Results with and without Controller

It is evident that balloon making productivity improves with the utilization of the ILC controller. The question now that still needs to be answered is: can this algorithm be applied to a batch of tubing extruded by a different company?

7.2.3 ILC Algorithm with a Different Brand of Tubing for 3 x 15mm Balloons

This section aims to test the reliability of the ILC controller on a different batch of extruded tubing. The new batch, made from Extrusioneering, has characteristics somewhat similar to the batch tested previously.

	Old Tubing for 3mm Balloon	New Tubing for 3mm Balloon
COMPANY	Innovative Extrusions	Extrusioneering
MATERIAL	Pebax	Pebax
DUROMETER	72D	72D
DIMENSIONS	0.036" x 0.0195" x 6'	0.036" x 0.020" x 6'
QUANTITY	1000 ft	1000 ft
LOT NUMBER	FP031904-001	050329-1-A
PURCHASE ORDER	10396	0012645

Table 7-3 Comparison of Tubing Batches Used to Blow 3 mm Balloons

The purpose of making new balloons and running more experimental tests is to verify whether or not the brand of extruded tubing plays a significant role in the outcome of balloon performance.

A total of twenty angioplasty balloons are blown using the Balloon Forming Machine. As done in the previous two experiments, ten are made with the aid of the ILC algorithm whereas the remaining balloons are made using the trial-and-error method. Once again, the burst pressure is set at 23.50 atmospheres (2.38 MPa), the double-wall thickness at 0.0014 inches (0.0356 mm), and the maximum diameter at 3.80 mm. It is immediately apparent by looking at the graphs below that the algorithm does not work as well with the second batch from Extrusioneering. The results below show that the traditional trial-and-error method is just as effective as the ILC algorithm since the controller is unable to produce balloons with the desired performance characteristics.

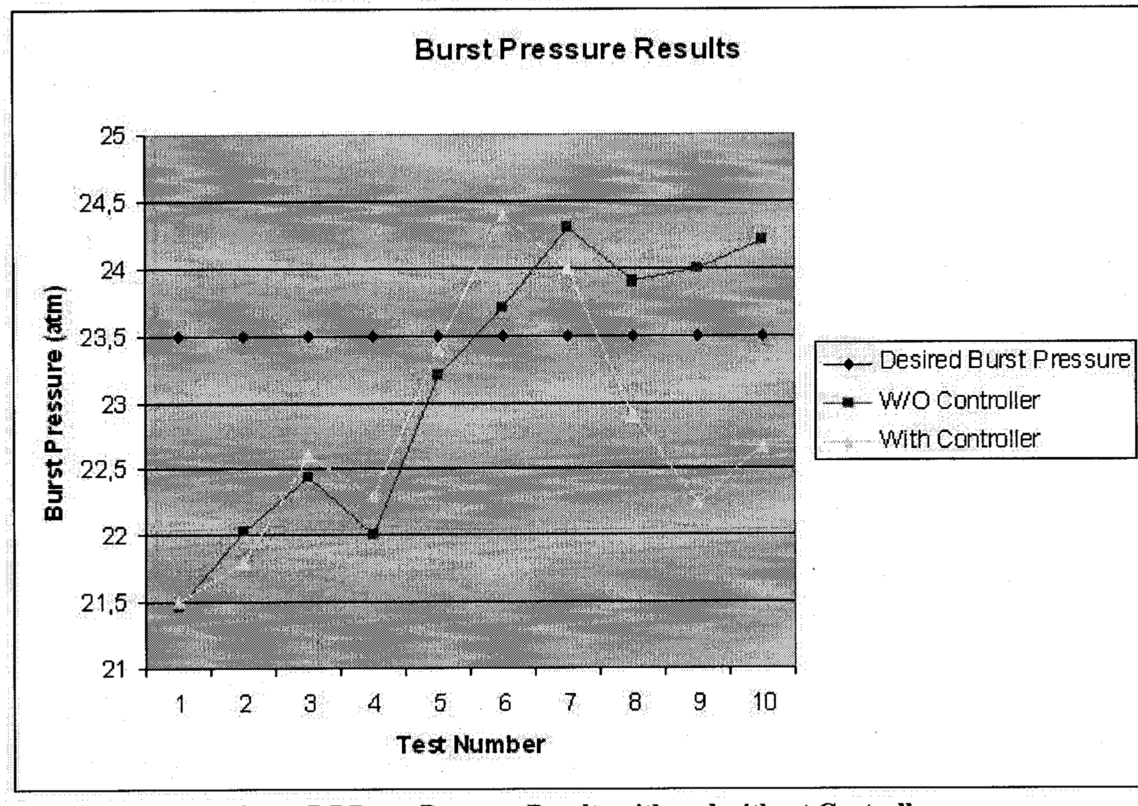


Figure 7-7 Burst Pressure Results with and without Controller

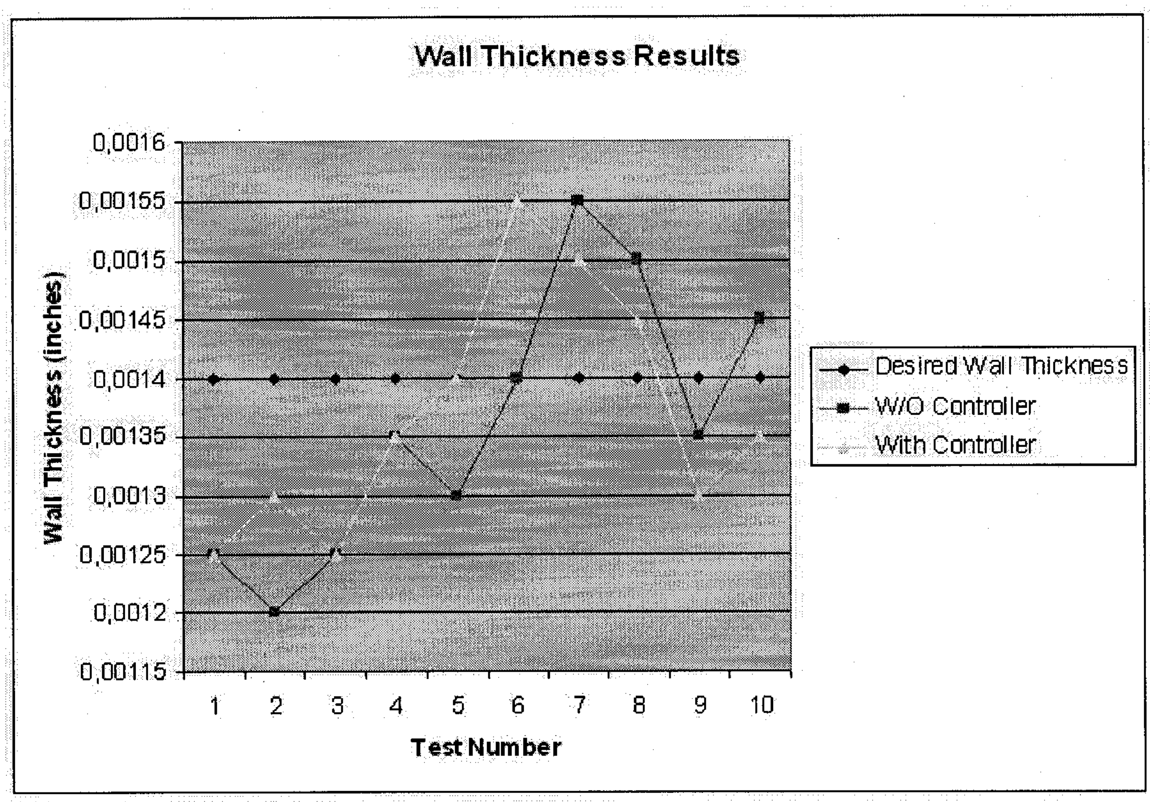


Figure 7-8 Double Wall Thickness Results with and without Controller

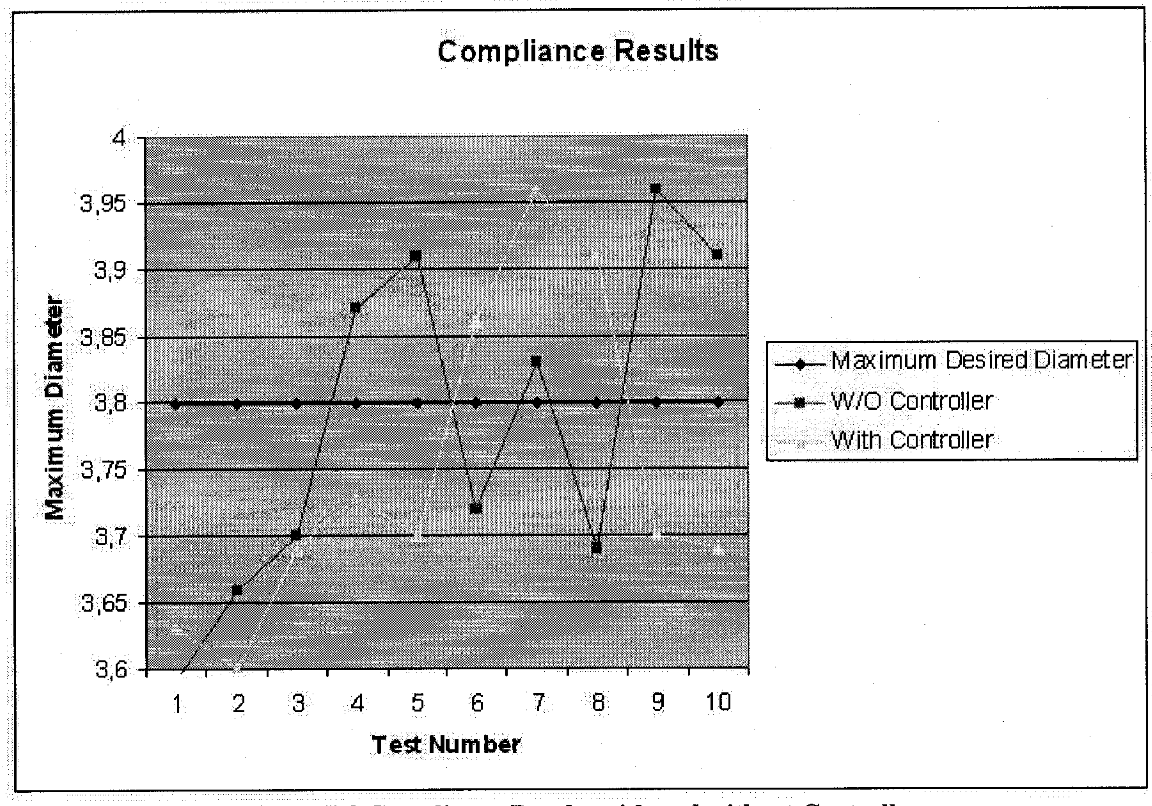


Figure 7-9 Compliance Results with and without Controller

It is also obvious that the devised model, or the 'A' matrix, is based on the *original* batch and must be redesigned to define *each* new tubing brand.

The results obtained from the two brands of tubing vary significantly. Even though the tubing appears identical (same material, durometer, etc) it is apparent that there are differences in the way Innovative Extrusion and Extrusioneering extrude their tubing. It is safe to say then that extrusion brand has a big impact on a balloon's final performance characteristics. Fundamentally each tubing brand will require its own ILC algorithm design.

8 CONCLUSION

The ILC algorithm functions reasonably well for a given batch of tubing in recommending the inputs to be entered into the Balloon Forming Machine. If a balloon needs to be slightly thinner or more compliant, the ILC algorithm suggests the inputs that are likely to produce those changes. The implementation of this controller can help reduce the number of trials needed to make specification grade angioplasty balloons, and it does so with less wasted material, less energy consumption and an increase in the production yield.

There is, however, one question that has not been answered. What happens when another batch of material from another manufacturer has to be ordered? The last chapter showed that the ILC algorithm did not correctly predict new inputs for the Balloon Forming Machine with a new batch of tubing. Although the second batch of tubing was supposed to be equivalent to the original batch, the results varied greatly for 3 mm balloons. The ILC algorithm that predicted inputs so well for one batch now failed by a considerable margin with another batch of tubing.

Evidently there are other parameters that need to be considered when modeling the balloon forming process. Room temperature and relative humidity in the laboratory, for example, are two such parameters. Results in a room that is warmer and more humid will differ from one that is a bit cooler and drier. Pebax® tubing absorbs humidity quite easily, and water content in the tubing changes its properties. Other factors may be the BFM operating parameters such as the force applied when stretching the tubing and the stretch speed. The addition of these parameters could improve the ILC algorithm.

Lastly, and probably the most important parameter, is the extrusion process. Two batches of tubing extruded from the same material and with the same hardness are rarely identical. The rotational speed of the gear pump or the temperature of the cooling bath are additional parameters that should be considered in order for the ILC algorithm to adapt to different batches of tubing.

The question that remains is “can a complex process such as the forming of angioplasty balloons be controlled by monitoring only a few significant variables and omitting others?” A simple controller can be devised to help reduce the operating time. However, such a controller cannot achieve universality as to batch changes and machine operating variations so as long that the parameters governing these variations are not inserted in the ILC algorithm model. Is the entire balloon forming process, starting from the extrusion of tubing, to the formation of a parison on the Double End Stretcher, and finally to the Balloon Forming Machine realistic to model? Would such a model be too complex? It is for this reason that the blow-molding of angioplasty balloons still relies on operator experience in the absence of a reliable universal controller.

8.1 Recommendations for Future Work

The proposed ILC algorithm provides satisfactory results when restricted to one batch of tubing because it does not consider the parameters associated with the manufacturer, extrusion process, room conditions and water content of different batches. In order to improve this algorithm a lot more testing is needed to determine the impact of the additional parameters. Only then we will be able to design an algorithm that can recommend inputs that result in convergent outputs for any batch of tubing material within specification.

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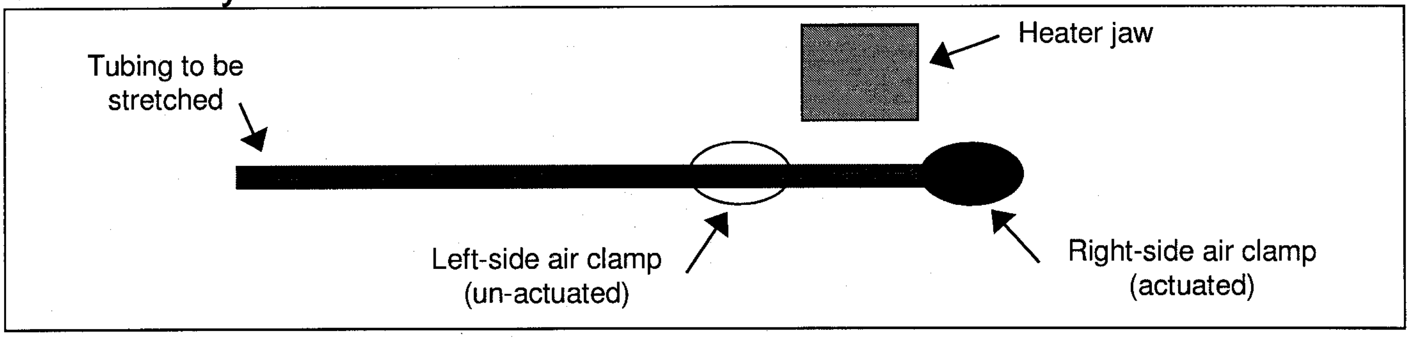
10 APPENDIX A

The schematics on the following pages illustrate the step-by-step procedure to follow while stretching tubing in the biomedical laboratory at CNRC-NRC IMI. The illustrations were done by Zoe Sarrat-Cave.

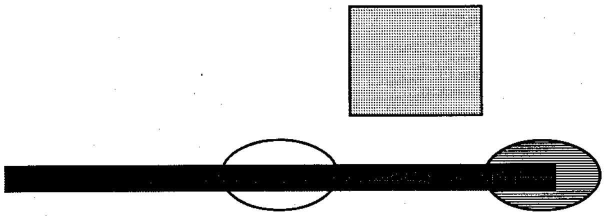
Starting up the DES

- Homing the system:
  - With the power on, the operator homes the device to the start position by pressing the “SAFETY” and “RESET” buttons simultaneously.
- Inserting the tube:
  - Operator activates the right-side air-powered clamp after manually inserting the tubing.
  - The left-side air-powered clamp is activated automatically during the stretching sequence.
- Begin sequence:
  - Operator initiates stretch sequence by pressing the “SAFETY” and “START” buttons simultaneously.

Guide To Symbols

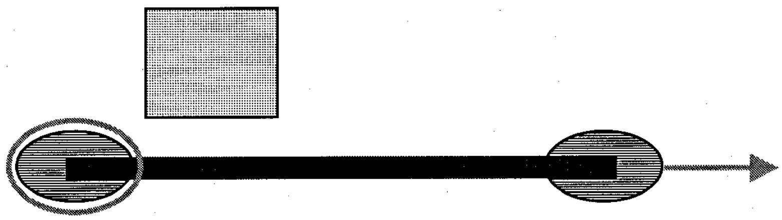


Step-by-Step DES Protocol

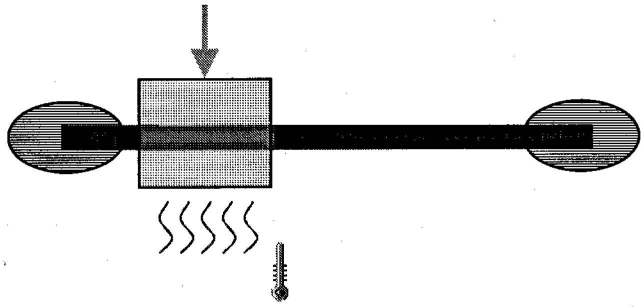


(Home position)

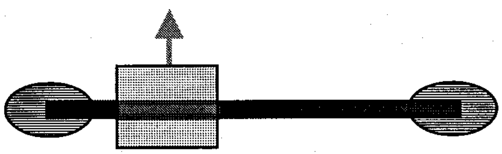
1. Right-side clamp assembly moves right to feed twice the heater width of tubing (146mm) plus the **UNSTRETCHED LENGTH** parameter setting. Left-side clamp actuates. The sequence first continues according to the left-side parameter settings.



2. Heater assembly moves in and jaw closes around tubing to begin heating for the amount of time specified by the **HEAT TIME** parameter setting. Heating occurs at the **TEMPERATURE** set on the OMRON temperature controllers.

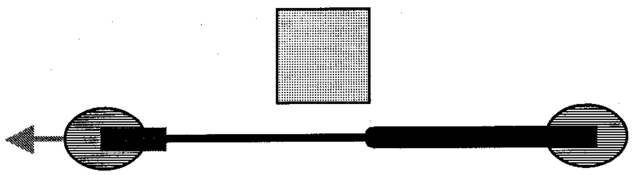


3. If **JAW CLOSED** parameter is set to "NO" for the left side, the heater jaw opens and the heater assembly retracts away from the tubing; otherwise the jaw remains closed around the tubing.

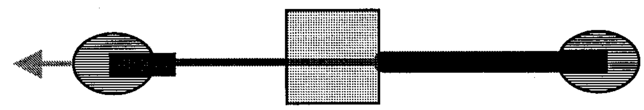


OR

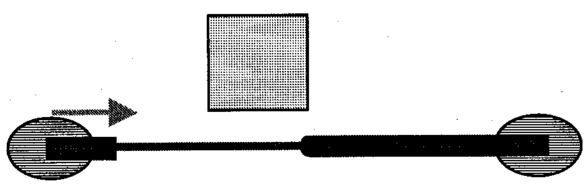
4. Left-side clamp assembly moves left at the set **STRETCH SPEED** and the corresponding **STRETCH DISTANCE** setting. This creates the proximal side of the parison.



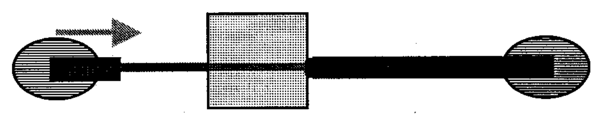
OR



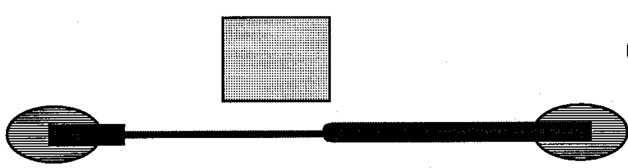
5. Left-side clamp assembly moves right a distance corresponding to the **RELAX BEFORE COOL** setting.



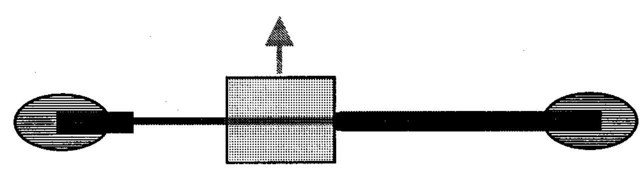
OR



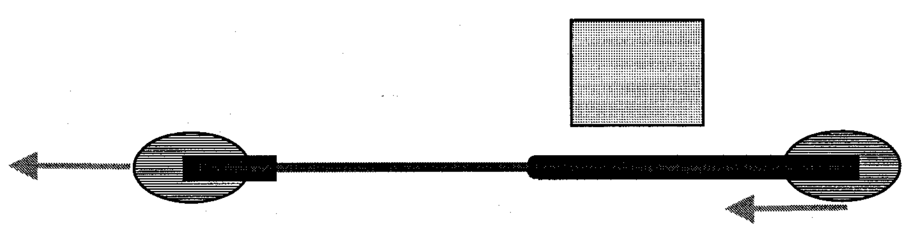
6. If the heater jaw is closed it now opens and retracts.



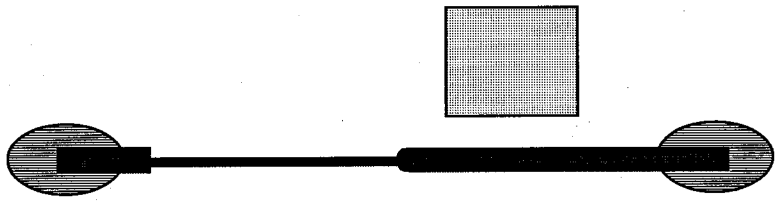
OR



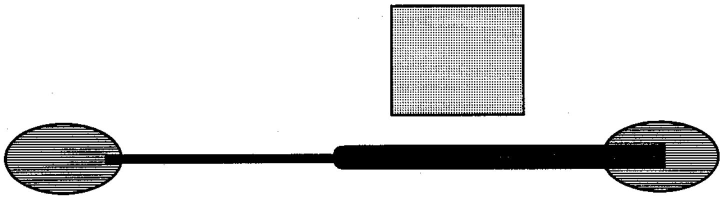
7. Left and right-side clamp assemblies move synchronously left to position the parison for heating on the right distal) side.



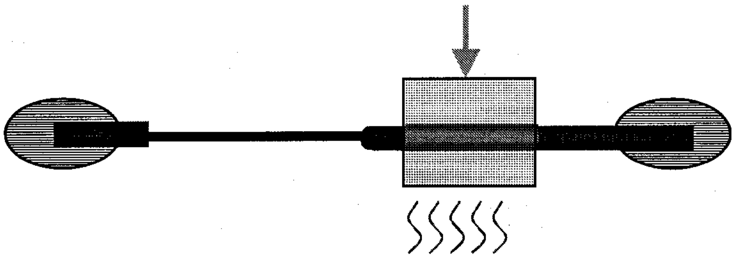
8. If **AIR COOL** is set to "YES", air is blown across the parison for the specified **COOLING TIME**.



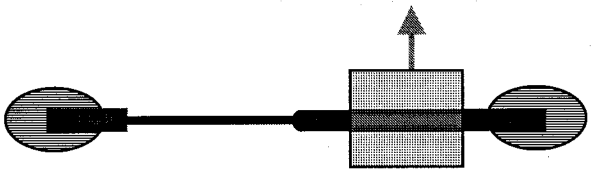
9. The left-side clamp assembly moves right the distance specified by the **RELAX AFTER COOL** parameter setting.



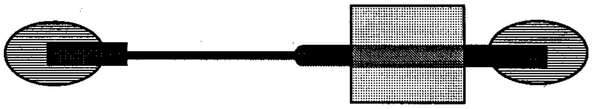
10. Heater assembly moves in and the jaw closes around tubing to begin the second heating cycle on the right side of the tube for time specified by the **HEAT TIME** parameter. The sequence now continues according to the right-side parameter settings. Heating occurs at the **TEMPERATURE** set on the OMRON temperature controllers.



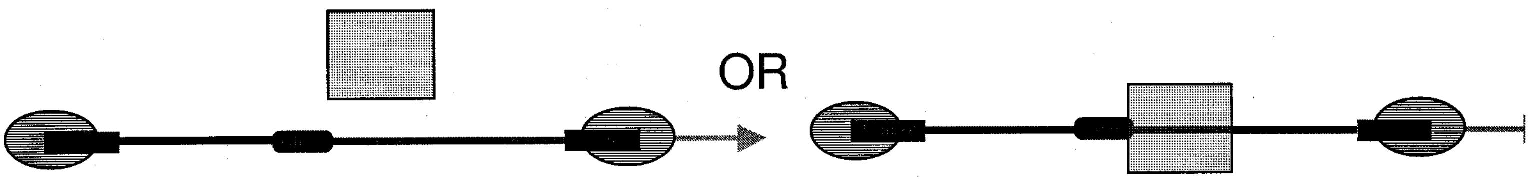
11. If **JAW CLOSED** parameter is set to "NO", the heater jaw opens and the heater assembly retracts away from the tubing; otherwise the jaw remains closed around the tubing.



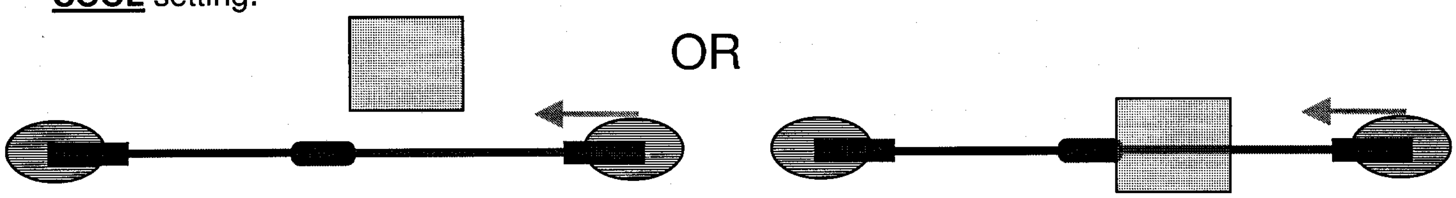
OR



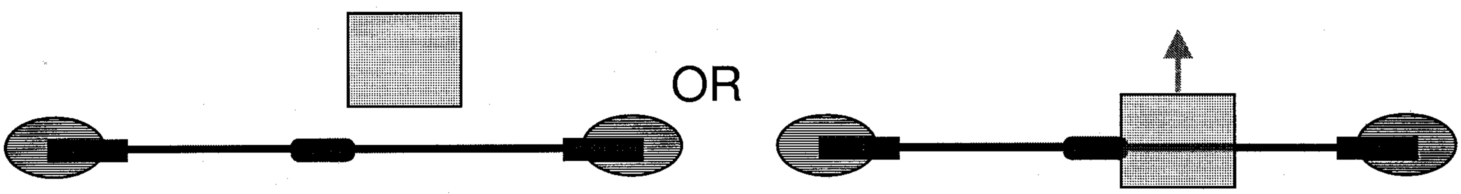
12. Right-side clamp assembly moves right the corresponding **STRETCH DISTANCE** parameter setting. This creates the distal side of the parison.



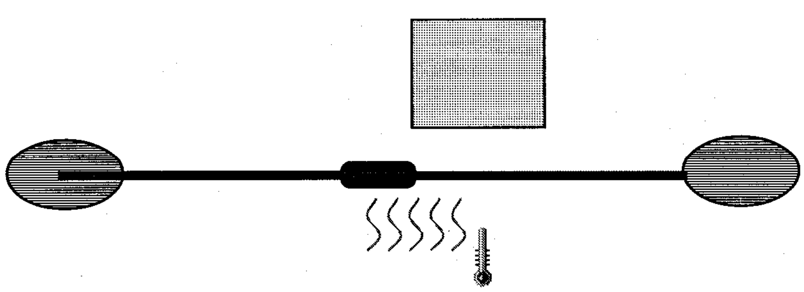
13. Right-side clamp assembly moves left a distance corresponding to the **RELAX BEFORE COOL** setting.



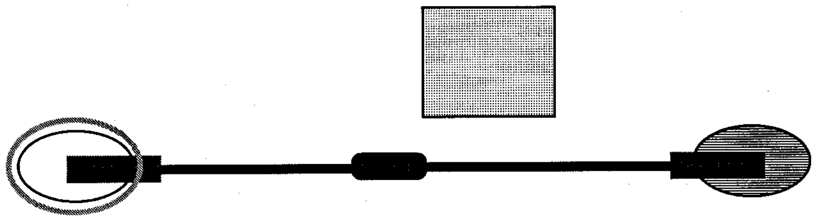
14. If the heater jaw is closed it now opens and retracts.



15. If **AIR COOL** is set to "YES" air is blown across the parison for the specified **COOLING TIME**.



16. When the cool time has elapsed, the left air clamp releases, and the sequence is complete. The operator manually releases the right-side clamp and removes the tubing.



11 APPENDIX B

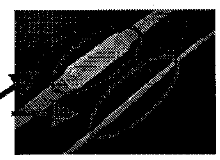
Step-by-Step BFM Protocol

Appendix B explains the protocol in detail used in the biomedical laboratory at CNRC-NRC IMI to form angioplasty balloons. The first step is the preparation of the tubing for the Balloon Forming Machine.

Tube Preparation

Creating the parison

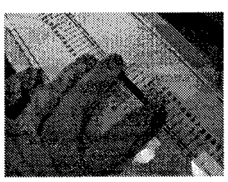
- Create parison with DES sequence (3mm, 8mm, etc)
- Mark both ends of the parison with pen



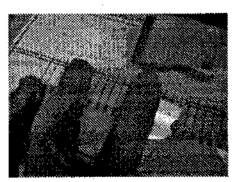
Parison
(or pre-form)

Preparing pre-formed tube

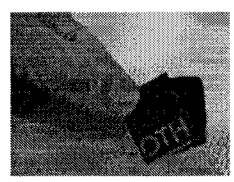
- Centre parison on "zero" line of graduated cutting board (proximal end on left)
- Trim proximal (left) end to 155mm
- Roughen surface of proximal (left) end with sand-paper to ensure good grip in chuck



Centre parison



Cut proximal (left) side to 155mm



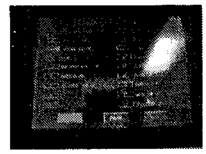
Roughen proximal end (~1 inch)

Once this task is done, the tubing is ready for insertion into the BFM. A guide with explanatory symbols is shown on the next page.

Start-Up

Starting the System:

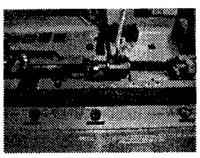
- With power ON select sequence (1 to18)
- Home machine by pressing "HOME" on touch screen
- Begin sequence by pressing "RUN" on touch screen



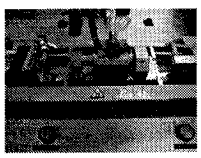
BFM Touch Screen

Steps 1,2,3: Load Pre-Formed Tube

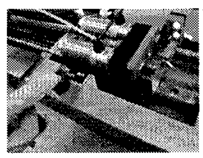
- To run **Step 1** press "SAFETY" and "RESET". Chuck, clamp and end-plugs move in to centre-mold.
- Load proximal end of tube into chuck and manually actuate chuck
- Feed distal end of tube through both end-plugs and centre-mold
- Run **Step 2** by pressing "START", chuck moves further in towards centre-mold
- Load distal end of tube into clamp and manually actuate clamp
- Run **Step 3** and begin balloon-forming process by pressing "START"



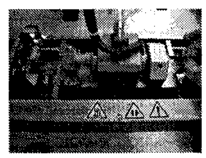
Home position



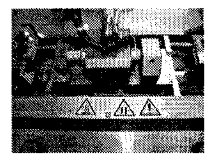
End-plugs and clamps move in



Load chuck

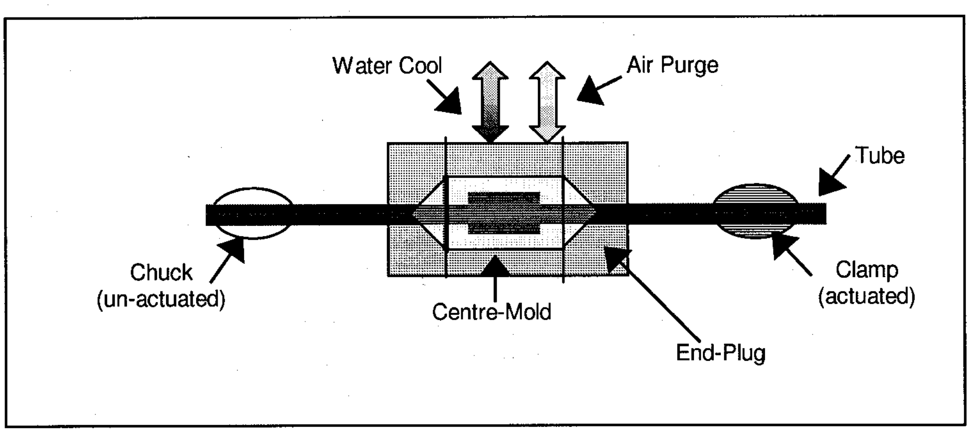


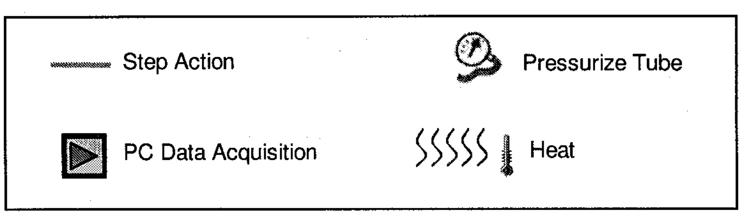
Feed tube through mold



Tube clamped, ready for balloon formation

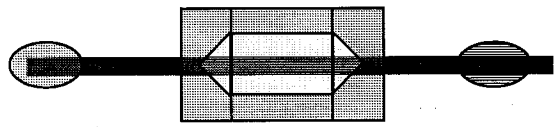
Guide to Symbols





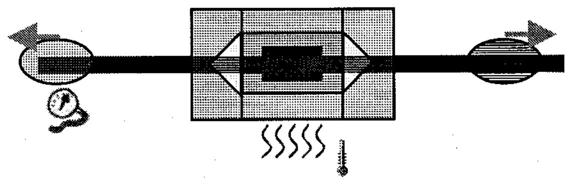
Balloon Forming Process

Tubing Loaded in Machine:



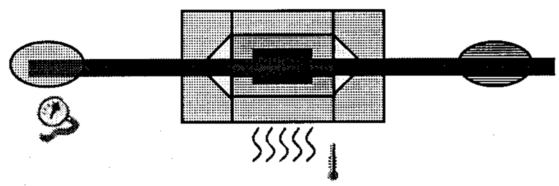
Step 4: Primary Heat, Pre-Stretch

- Axially pre-stretch both ends of tube (~1mm)
- Heat centre-mold (and end-plugs for 8mm)
- Pressurize tube
- Exit condition TIME



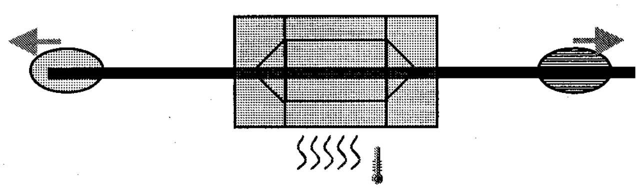
Step 5: Data Acquisition

- Activate PC tracking
- Exit condition TIME



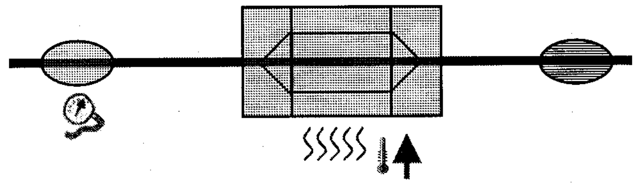
Step 6: Form Balloon

- Axially stretch both ends of heated, pressurized tube to specified distance
- Heated parison expands to form balloon in centre-mold
- Exit condition TIME (long enough for data collection)



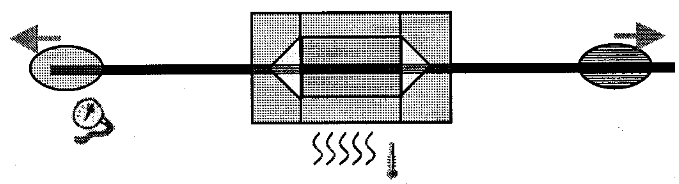
Step 7: Heat Balloon

- Increase temperature of mold
- Exit condition TEMPERATURE (set less than BALLOON FORMING TEMP to increase rate of heating)



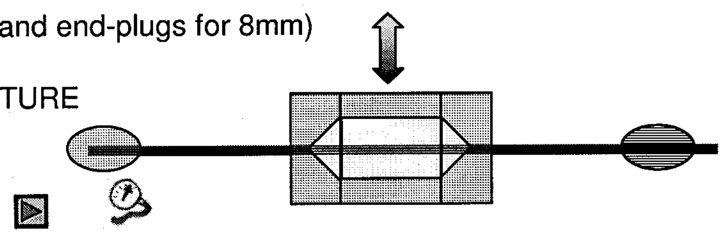
Step 8: Secondary Stretch

- Axially stretch both ends of tube to specified distance
- Forms cones of balloon by pulling material into end-plugs
- Exit condition TEMPERATURE (set less than BALLOON FORMING TEMP for control of max temp achieved)



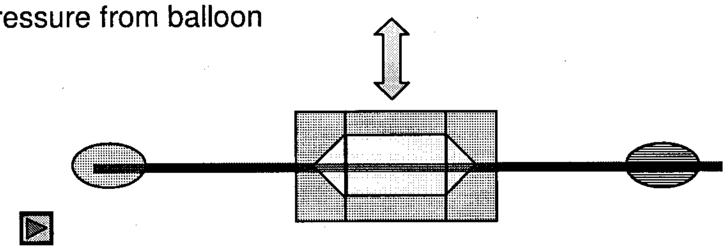
Step 9: Mold Cooling

- Water cool centre-mold (and end-plugs for 8mm)
- Maintain pressure
- Exit condition TEMPERATURE



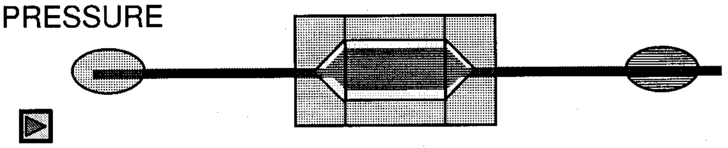
Step 10: Mold Purge

- Purge water from mold with air flow
- Open valve to remove pressure from balloon
- Exit condition TIME



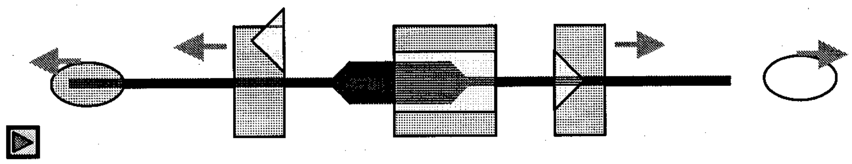
Step 11: Evacuate balloon

- Dump air pressure from balloon
- Exit condition PRESSURE



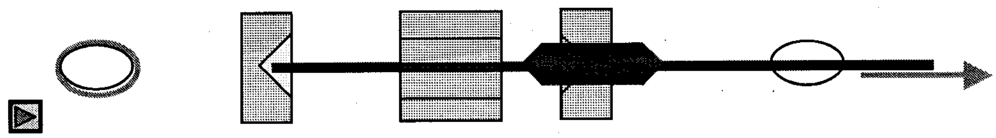
Steps 12: Clamp release, mold open

- Mold opens and clamp releases. Chuck, clamp and end-plugs retract away from centre-mold.



Steps 13: Remove balloon

- Manually release chuck and remove balloon from mold (pull proximal end through centre-mold, distal end through right end-plug)



12 APPENDIX C

The following pages contain the MATLAB files used to calculate the ILC algorithm for the 3 mm and 8 mm angioplasty balloons.

```
% Dominic Lalli
% Student I.D.#: 119930377
% Professor Benoit Boulet

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
% This program prompts the user to enter the desired outputs for a 3mm
% angioplasty balloon and returns inputs to be entered in the BFM.
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

clear all;

% Results are shown in 'long' format
format long;

% 'A' Matrix
A1 = [-0.35  0.065   -0.09   -0.85     0.4;
     -25e-6   0        0    -25e-6     0;
     -25e-3 0.004   -0.004  -0.0035   0.01];
% Scaling matrix
A2 = [1  0   0;0 10000 0; 0 0 1];

% New 'A' matrix
A = A2*A1

% Finding the pseudoinverse of matrix A
A_pseudo = pinv(A);

% Including pertubations
% Forms a 3x5 random matrix with entires from -1 to 1
random = 2*(rand(3,5)-0.5)

% Delta matrix with 10% error
Delta = random.*(0.1*A)

% New 'A' matrix with pertubations
A_pert = A + Delta

% Prompts the user to enter desired burst presure
Pressure = input('Please enter the desired burst pressure (15 to 28 atm):');
while ((Pressure < 15) | (Pressure > 28))
    Pressure = input('Please re-enter a new value:');
end

% Prompts the user to enter desired double-wall thickness
Thick = input('Please enter the desired double-wall balloon thickness (0.0012 to 0.0017 i ↙
nches):');
while ((Thick < 0.0012) | (Thick > 0.0017))
    Thick = input('Please re-enter a new value:');
end

%Prompts user to enter maximum desired diameter before burst
Diameter = input('Please enter the maximum desired diameter (3.3 to 4.7 mm):');
while ((Diameter < 3.3) | (Diameter > 4.7))
    Diameter = input('Please re-enter a new value:');
end

% Displays the chosen outputs before calculating the inputs
```

```
disp('The chosen values for the burst pressure, double-wall thickness, and Maximum diamet ↙
er are:');
disp('hit any key to continue...');
pause
Pressure
pause
Thick
pause
Diameter
pause

% Starting point to calculate necessary inputs
u_init=[33;65;55;13.5;15];

% Optimal inputs from laboratory experiments which make nice balloons
u_opt = [35;60;60;13.5;15];

% Results obtained from optimal inputs
% Results are burst pressure is 23.2 atm, double-wall thickness is
% 0.0015 inches and maximum diameter before burst is 3.84mm
y_opt = [23.2;0.0015;3.84];

% Calculating the differences in the initial strating point and the optimal
% inputs
delta_u = u_init - u_opt;

% Calculates the theoretical output to u_init
y = A*delta_u + A2*y_opt;

% Setting u_final to u_init
u_final = u_init;

% Setting temp to zero
temp = 0;

% Starting point for desired output
y_new = [24.025;15;3.89];

% Setting y_final to y_new
y_final = y_new;

% Gain matrix is the identity matrix
Ki = eye(5);

% Unit of 'Thickness' will be in 1/10000 of an inch
Thickness = Thick*10000;

% Setting the desired ouputs which the user entered
y_des = [Pressure;Thickness;Diameter];

% Setting y_next to y
y_next= y;

% Performs the IILC algorithm
for k=1:2
    temp = u_init + Ki*A_pseudo*(y_des - y_next);
    u_final = [u_final temp]
```

```
    u_init = u_final(:,k+1);
    y_next = A_pert*(temp-u_opt)+A2*y_opt;
    y_final = [y_final y_next]
    y_next = y_final(:,k+1)
    pause
end

% Displays the recommended inputs
disp('To achieve these outputs, the IILC recommends setting your inputs to:');
disp('hit any key to continue...');
pause
disp('Applied Pressure in atm:');
u_init(1)
if ((u_init(1) < 33) | (u_init(1) > 39))
    disp('The pressure falls out of desired pressure range.');
    disp('Please retry once again to obtain a valid applied pressure input');
end
pause
disp('Mold Temperature in deg C:');
u_init(2)
if ((u_init(2) < 55) | (u_init(2) > 65))
    disp('The temperature falls out of desired temp. range.');
    disp('Please retry once again to obtain a valid temperature input');
end
pause
disp('Heat Time in seconds:');
u_init(3)
if ((u_init(3) < 50) | (u_init(3) > 65))
    disp('The heat time falls out of desired time range.');
    disp('Please retry once again to obtain a valid heat time input');
end
pause
disp('Stretch Distance in mm:');
u_init(4)
if ((u_init(4) < 12.5) | (u_init(4) > 15.5))
    disp('The stretch distance falls out of desired stretch range.');
    disp('Please retry once again to obtain a valid stretch distance input');
end
pause
disp('Parison Length in mm:');
u_init(5)
if ((u_init(5) < 13) | (u_init(5) > 18))
    disp('The parison length falls out of desired length range.');
    disp('Please retry once again to obtain a valid parison length input');
end
```

```
% Dominic Lalli
% Student I.D.#: 119930377
% Professor Benoit Boulet

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
% This program prompts the user to enter the desired outputs for a 8mm
% angioplasty balloon and returns inputs to be entered in the BFM.
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

clear all;

% Results are shown in 'long' format
format long;

% 'A' Matrix
A1 = [0.1475    0.0295      -0.025      -0.0775    0.1125
     -0.000025  -2.5E-06    -2.5E-06    -0.000025  0
      0.0325    0.0035      -0.012       -0.08      0.01];

% Scaling matrix
A2 = [1  0   0;0 10000 0; 0 0 1];

% New 'A' matrix
A = A2*A1

% Finding the pseudoinverse of matrix A
A_pseudo = pinv(A);

% Including pertubations
% Forms a 3x5 random matrix with entires from -1 to 1
random = 2*(rand(3,5)-0.5)

% Delta matrix with 10% error
Delta = random.*(0.1*A)

% New 'A' matrix with pertubations
A_pert = A + Delta

% Prompts the user to enter desired burst presure
Pressure = input('Please enter the desired burst pressure (12 to 17 atm):');
while ((Pressure < 12) || (Pressure > 17))
    Pressure = input('Please re-enter a new value:');
end

% Prompts the user to enter desired double-wall thickness
Thick = input('Please enter the desired double-wall balloon thickness (0.0020 to 0.0029 i ↙
nches):');
while ((Thick < 0.0020) || (Thick > 0.0029))
    Thick = input('Please re-enter a new value:');
end

%Prompts user to enter maximum desired diameter before burst
Diameter = input('Please enter the maximum desired diameter (8.8 to 10.8 mm):');
while ((Diameter < 8.8) || (Diameter > 10.8))
    Diameter = input('Please re-enter a new value:');
end
```

```
% Displays the chosen outputs before calculating the inputs
disp('The chosen values for the burst pressure, double-wall thickness, and Maximum diamet ↙
er are:');
disp('hit any key to continue...');
pause
Pressure
pause
Thick
pause
Diameter
pause

% Starting point to calculate necessary inputs
u_init=[27;70;130;27;27];

% Optimal inputs from laboratory experiments which make nice balloons
u_opt = [24;70;140;30;25];

% Results obtained from optimal inputs
% Results are burst pressure is 23.2 atm, double-wall thickness is
% 0.0015 inches and maximum diameter before burst is 3.84mm
y_opt = [16.12;0.00255;10.44];

% Calculating the differences in the initial strating point and the optimal
% inputs
delta_u = u_init - u_opt;

% Calculates the theoretical output to u_init
y = A*delta_u + A2*y_opt;

% Setting u_final to u_init
u_final = u_init;

% Setting temp to zero
temp = 0;

% Starting point for desired output
y_new = [16.24;26;10.53];

% Setting y_final to y_new
y_final = y_new;

% Gain matrix is the identity matrix
Ki = eye(5);

% Unit of 'Thickness' will be in 1/10000 of an inch
Thickness = Thick*10000;

% Setting the desired ouputs which the user entered
y_des = [Pressure;Thickness;Diameter];

% Setting y_next to y
y_next= y;

% Performs the IILC algorithm
for k=1:2
    temp = u_init + Ki*A_pseudo*(y_des - y_next);
```

```
    u_final = [u_final temp]
    u_init = u_final(:,k+1);
    y_next = A_pert*(temp-u_opt)+A2*y_opt;
    y_final = [y_final y_next]
    y_next = y_final(:,k+1)
    pause
end

% Displays the recommended inputs
disp('To achieve these outputs, the IILC recommends setting your inputs to:');
disp('hit any key to continue...');
pause
disp('Applied Pressure in atm:');
u_init(1)
if ((u_init(1) < 22) | (u_init(1) > 26))
    disp('The pressure falls out of desired pressure range.');
    disp('Please retry once again to obtain a valid applied pressure input');
end
pause
disp('Mold Temperature in deg C:');
u_init(2)
if ((u_init(2) < 50) | (u_init(2) > 80))
    disp('The temperature falls out of desired temp. range.');
    disp('Please retry once again to obtain a valid temperature input');
end
pause
disp('Heat Time in seconds:');
u_init(3)
if ((u_init(3) < 130) | (u_init(3) > 150))
    disp('The heat time falls out of desired time range.');
    disp('Please retry once again to obtain a valid heat time input');
end
pause
disp('Stretch Distance in mm:');
u_init(4)
if ((u_init(4) < 28) | (u_init(4) > 32))
    disp('The stretch distance falls out of desired stretch range.');
    disp('Please retry once again to obtain a valid stretch distance input');
end
pause
disp('Parison Length in mm:');
u_init(5)
if ((u_init(5) < 21) | (u_init(5) > 27))
    disp('The parison length falls out of desired length range.');
    disp('Please retry once again to obtain a valid parison length input');
end
```