Studies of Poly(vinyl chloride) Based Endotracheal Tubes From the Nano- to Macroscopic Scale

Kristin Rebecca Brodie

Submitted to the Department of Materials Science and Engineering
in Partial Fulfillment of the Requirements for the Degree of

Bachelor of Science

at the

Massachusetts Institute of Technology

May 2003

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Abstract

The endotracheal tube (ET) is a polymeric conduit that forms a closed system of pulmonary ventilation that is most often used to allow delivery of air to critically ill patients via intubation. Currently used ETs cause a wide variety of clinical problems including laryngeal edema (inflammation) and occasionally death. To investigate the origins of this behavior, mechanical, chemical, morphological, and biocompatibility characterization of injection-molded (Endotrol) tubes of poly(vinyl chloride) (PVC) containing ~35 wt% di-ethylhexyl phthalate (DEHP) plasticizer was conducted. Experiments were performed on a nano- to macroscale. The following techniques were used in analysis: fourier-transform infrared spectroscopy, gel permeation chromatography, differential scanning calorimetry, accelerated solvent extraction, uniaxial tensile testing, high-resolution force spectroscopy, atomic force microscopy, scanning electron microscopy, and plasticizer leaching. Detailed processing-structure-property relationships will be formulated based on these experimental results. The polymeric materials used in endotracheal tubes have never before been analyzed in such a manner, and the research performed may lead to dramatic results that would forever change the field of biomedical device manufacturing and greatly decrease related patient injury. The results of these studies are intended to form the basis for future ET materials selection and design.

Thesis Supervisor: Professor Christine Ortiz
Title: Assistant Professor of Materials Science and Engineering

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Acknowledgements

I would like to thank Dr. Everard Cox (Maryland Institute for Emergency Medicine) for his inspiration in the founding of this project. I want to thank Prof. Christine Ortiz for her support and guidance. I would like to give my appreciation to the members of the Ortiz Polymer Laboratory Group for their assistance, suggestions and aid. I would like to lend appreciation to Prof. Mary Boyce, Prof. Anne Mayes, Prof. David Roylance, Saul Griffiths (MIT Media Lab), Tim McClure(CMSE), Michael Frongillo (CMSE-SEM) and all the many graduate students who assisted me in my research. I would also like to thank the Dionex Corporation and the Boston Center for Medical Simulation for their time, help and facilities. This research project was funded in part by the National Science Foundation and the John Reed Foundation, a sponsor of the Undergraduate Research Opportunities Program at MIT.

1 INTRODUCTION

1.1 What are *endotracheal tubes?*

The **endotracheal tube** is a closed system of pulmonary ventilation most often used in critical intensive care situations to allow the delivery of air to the patient. In 1988, it was estimated that over 70 million endotracheal tubes were used yearly in patients requiring mechanical assistance in breathing. In 2000, that number has grown to an estimated 200 million intubations per year.[19] The endotracheal tube is a polymeric conduit between the lungs and a ventilator and is used to form a closed system necessary to maintain optimal respiration, as well as protect the lungs from any foreign material that may be aspirated into the trachea. The tracheal tube is inserted through the mouth, passes by the vocal chord region and into the trachea. The cuff, located near the bottom end of the tube at the trachea, is a spherical, thin-walled bag that is inflated with air until it completely seals off the passageway to the lungs. An artificial respiratory system (ventilator) is then attached to the system.[18] A picture of a typical endotracheal tube that has been inserted into a patient is shown below in **Figure 1.1**.

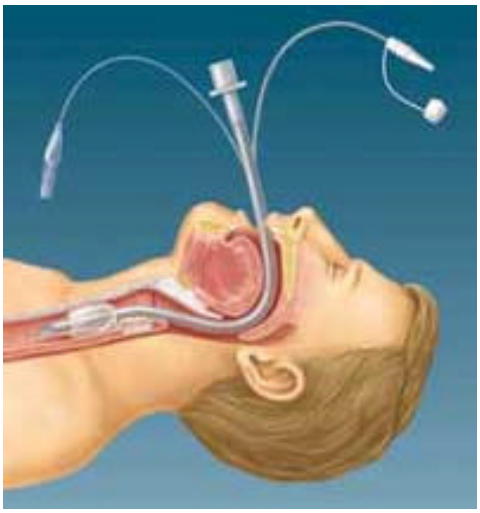


Figure 1.1 Illustration of an endotracheal tube in-patient
http://www.mallinckrodt.com/Respiratory/resp/Product/HiLoEvac/HiLoMini.html

1.2 Why study *endotracheal tubes?*

The first objective of this project was to gain a more complete understanding of the properties of the materials, i.e. both matrix and plasticizer, used in the current endotracheal tubes. The nano and macro properties of the PVC and plasticizer were analyzed. One endotracheal tube (Endotrol) was chosen as a model system. This particular ET was chosen because it is one of the newest models of endotracheal tubes on the market, and manufactured by one of the largest and most predominant medical device manufacturing companies. The Endotrol tube was studied by a variety of experimental techniques including mechanical properties (e.g. strength, stiffness, pressure), chemical composition (e.g. % PVC, plasticizer other additives), micro- and nanostructure (e.g. defects, polymeric chain molecular weight and alignment, surface roughness), and biocompatibility (e.g. surface forces measurement, plasticizer leaching). These experiments yielded appropriate processing-structure-property relationships of the polymeric materials necessary for the manufacturing of an endotracheal tube similar to those commercially available.

In addition, model samples of PVC with DEHP plasticizer have been made from well-defined constituent materials and the effect of plasticizer, processing parameters, geometry, etc. have been investigated. The PVC samples have been processed using an injection molding machine with a single-screw to mix the polymer. These samples have also been analyzed and tested and their properties compared with the commercial endotracheal tube samples. This thesis will demonstrate a thorough understanding of the properties of the current PVC and plasticizer used in commercial endotracheal tubes. The results found from this research will lay a foundation on which further material and design research can be performed to improve endotracheal tubes.

1.3 Properties of *endotracheal tubes*

Endotracheal tubes are currently manufactured by several major companies, the most prevalent are Mallinckrodt®, Sheridan® and Rusch®. After contacting these companies to ask about their endotracheal tubes, each claim to distribute endotracheal tubes made of some PVC/plasticizer compound, of which the particulars about exact PVC type, plasticizer(s) and weight percent used, the specific polymeric properties, and processing methods are proprietary. These three manufacturers of endotracheal tubes each produce tubes made with a similar design. Tubes, such as those shown in Figure 1.2, are currently used in common medical practice. The adult endotracheal tube design includes a curved tube, usually with a 6-9 mm diameter, with a small "Murphy's Eye" hole near the end of the tube and a thin, inflatable cuff near the tracheal region. The section of the tube which does not enter the body has a standard connector attached that fits to the respiratory device and a pilot balloon used to inflate the cuff.[1] Is this one continuous piece of material that is injection molded? indicate thicknesses, length, of each component, transparent

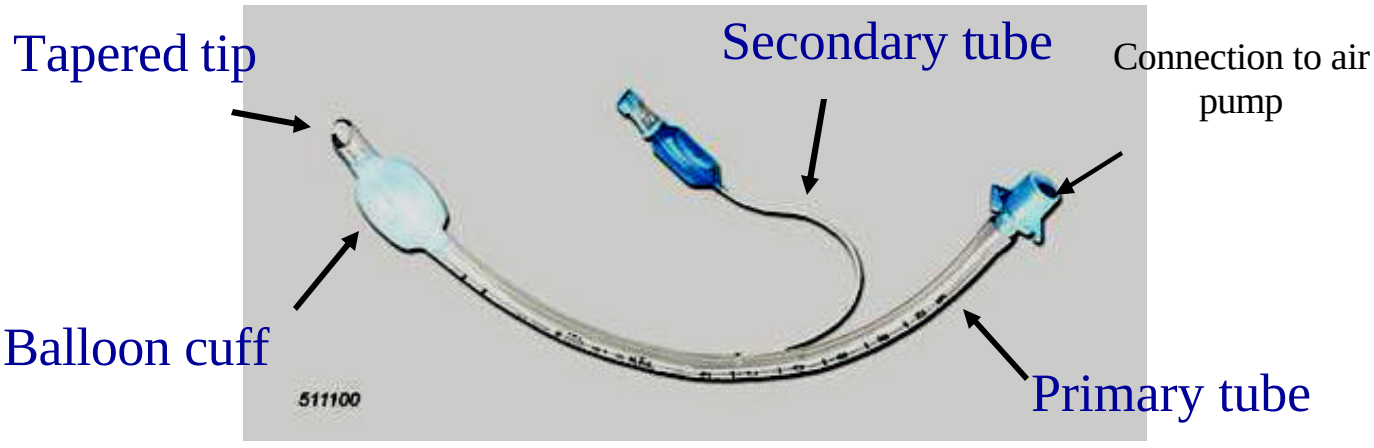


Figure 1.2. Current endotracheal tube http://www.kyoling.com/jingling/qc.htm

The endotracheal tubes currently used are primarily made up of poly(vinyl chloride) (PVC) combined with about 30-40 wt. % of low molecular weight plasticizers.[30] The chemical structure of PVC (shown below) is $[-CH_2CH(Cl)-]_n$, and the molecular weight range for medical grade PVC is generally very high, ranging from 120-200 kg/mol.

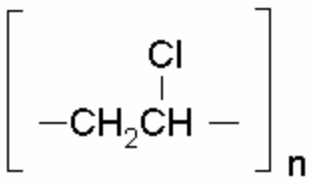


Figure 1.3. Chemical structure of poly(vinyl chloride)

The most common plasticizer combined with medical grade PVC in the construction of endotracheal tubes is di-ethylhexyl phthalate (DEHP), also referred to as di-octyl phthalate (DOP). The addition of plasticizer causes the PVC to become more supple and flexible while still maintaining mechanical strength, which are properties necessary for flexibility in the tube and cuff of endotracheal tubes.[27] The chemical formula for DEHP, presented in Figure 1.4, is $C_6H_4[CO_2CH_2(CH_2)_6CH_3]_2$, and the molecular weight is 394.60g/mol.[16]

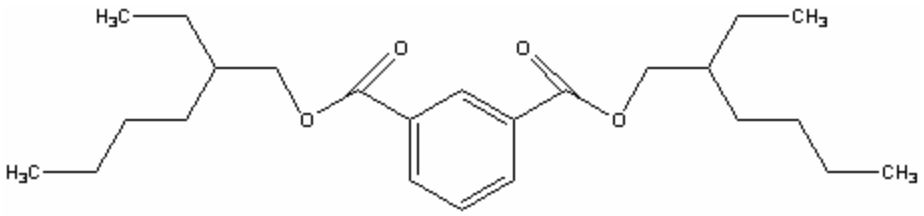


Figure 1.4. Molecule of Di-ethylhexyl phthalate

1.4 What are *problems* with current endotracheal tubes?

Despite the FDA's approval of DEHP in PVC for endotracheal tube manufacturing, many companies have been researching vinyl plastics and phthalates for their potential

hazards to patients. Poly (vinyl chloride), while medical grade claims 99.9% purity, may still contain vinyl monomers, which is hazardous to humans, carcinogenic? (ref). Phthalates have been under investigation due to their potential carcinogenic properties and irritation of mucus membranes. In addition to the separate threats posed by PVC and DEHP individually, the DEHP has a tendency to leach out of the PVC in products. This is another potential problem with the current materials being used to make in endotracheal tubes.[4]

There are some physical design problems with the endotracheal tubes, such as the high cuff pressure against the tracheal walls and effects on the tube materials due to length of intubation time that may be the cause of the wide range of problems found in patients. For years, the current tracheal tubes in use have been and continue to cause problems such as irritation and mild laryngeal edema to severe morbidity and occasionally death directly attributable to intubation.[7] In order to alleviate these problems, it would be necessary to have either a cuff that is not continuously at high pressure, or change the polymeric material in order to lessen the irritation or harm to the tracheal walls.

It is suspected that a key issue in the analysis of endotracheal tubes will be the molecular-scale intermolecular interactions between the small molecule additive components (e.g. plasticizers) and the higher molecular weight polymer matrix. The high molecular weight polymer matrix has a large influence on both the mechanical properties, and the chemical interactions with the surrounding biological tissue. By studying the current tracheal tubes and the micro and macro properties exhibited, a foundation on which further research can be performed will be made. From this point, alterations can be made to improve upon the current endotracheal tube, in materials and design.[24]

2 EXPERIMENTAL METHODS

The study of nano to macro-scale properties of endotracheal tubes was done using chemical and mechanical analysis techniques. The techniques and procedures used in testing are described in this section. Microscopic, chemical and mechanical analysis techniques employed are discussed in the following sections.

2.1 Surface Analysis

The study of the nanoscopic properties of current polymeric materials used in endotracheal tubes gives information about material design properties on the microscopic scale. Micro and nanostructure (e.g. defects, polymeric chain molecular weight and alignment, surface roughness) and biocompatibility (e.g. surface forces measurement, plasticizer leaching) test results give useful property information about the PVC and DEHP.

2.1.1 An **Optical Microscope** can be used to observe the microscopic surface features of polymeric materials. The *Axioskop 20*, Zeiss Inc. with transmitted and reflected light, differential interference contrast, cross-polarizers, and incident light fluorescence, is located in MIT Lab 12-065. The microscope is attached to a *KODAK Digital Science Microscopy Documentation System 100 (MDS 100)* in order to capture images of the samples at 2.5x, 10x, 40x and 100x.

An optical microscope was used to give a general idea of what the surface of the endotracheal tube cuff looks like. In order to view the transparent polymer samples, cuff and tube fragments were attached with 3M permanent double-sided tape onto glass microscope slides. The samples were placed beneath the microscope head, and transmitted

light filters and cross-polarizers were used to get more accurate images of the polymer surface.

2.1.2 Atomic Force Microscopy (AFM) The Multimode™ AFM is used as an all-purpose imaging tool for a variety of synthetic and biological materials. AFM has been used in air and fluids in tapping mode, contact mode, friction mode, force-volume, and force spectroscopy. The MultiMode™ system features two scanners, "EV" which has better control to image smaller sample sizes, and "JV" which is used for slightly larger samples. The JV scanner has scan ranges up to 120 μm on the X–Y axes, and a Z range up to 6 μm. The MultiMode™ is controlled with either the industry-standard NanoScope IIIa controller which provides 16-bit resolution on all three axes, with three independent 16-bit digital-to-analog converters (DACs) in X and Y for control of the scan pattern, scaling, and offset. This configuration provides 16-bit resolution of the lateral scanning motion at any scan size. [14]

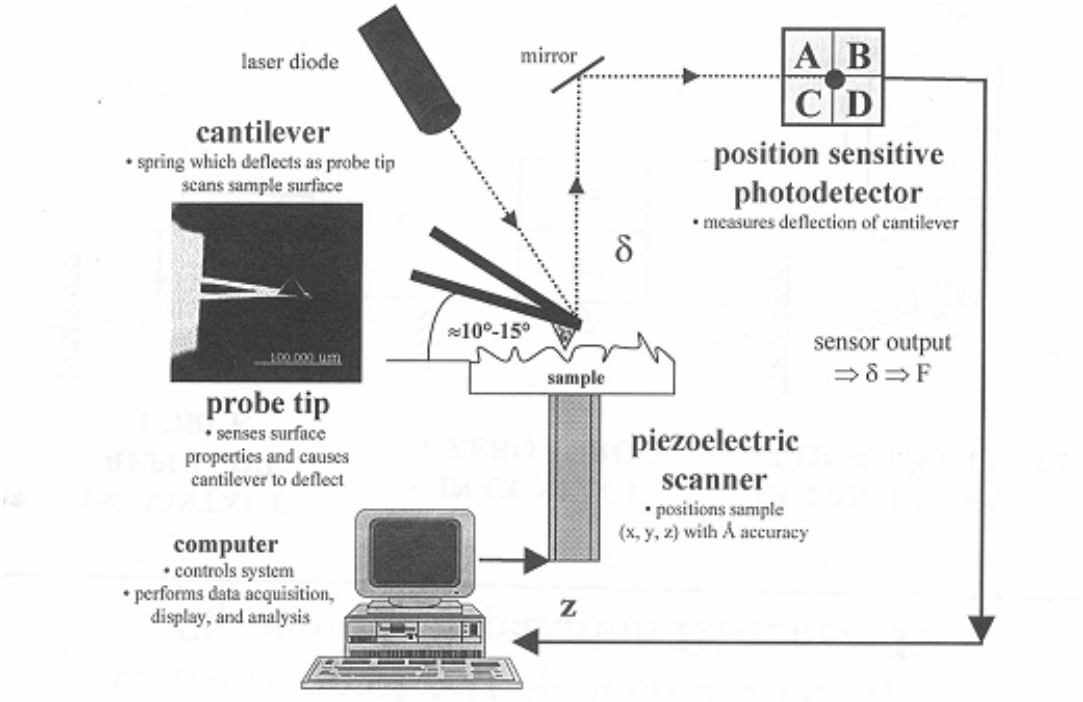


Figure 2.1 Flow chart showing operation and control feedback loop of AFM

The *Digital Instruments* NanoScope® IIIA System was used to take surface images of the polymer used in endotracheal tubes. Nanoscopic imaging was performed using contact mode AFM in air. Commercial endotracheal cuff samples, tube samples, and processed medical grade samples of PVC/plasticizer were attached to AFM 15mm diameter specimen disks using permanent double-sided tape. Deflection and height images were taken in order to view the surface features of the plastics.

2.1.3 Scanning Electron Microscopy shows detailed 3-D images at magnifications much higher than possible with an optical light microscope. Images are created without light waves and instead, electrically conductive samples are illuminated with electrons. SEM samples are coated with a thin layer of gold by a sputter coater. Samples are placed inside the microscope chamber, after which the air is pumped out of the chamber to create an air-tight vacuum chamber. The electron gun, located at the top of the microscope, emits a beam of high energy electrons which travel down through a series of magnetic lenses to a set of scanning coils which move the beam back and forth across the specimen. As the electrons hit locations on the sample, secondary electrons are loosed and detected, counted, and a signal is sent to the amplifier. From this reading, a surface image can be built. The Scanning Electron Microscope helps to reveal new levels of detail and complexity of biological and synthetic structures. Figure 2.2 demonstrates the concepts described above.[16]

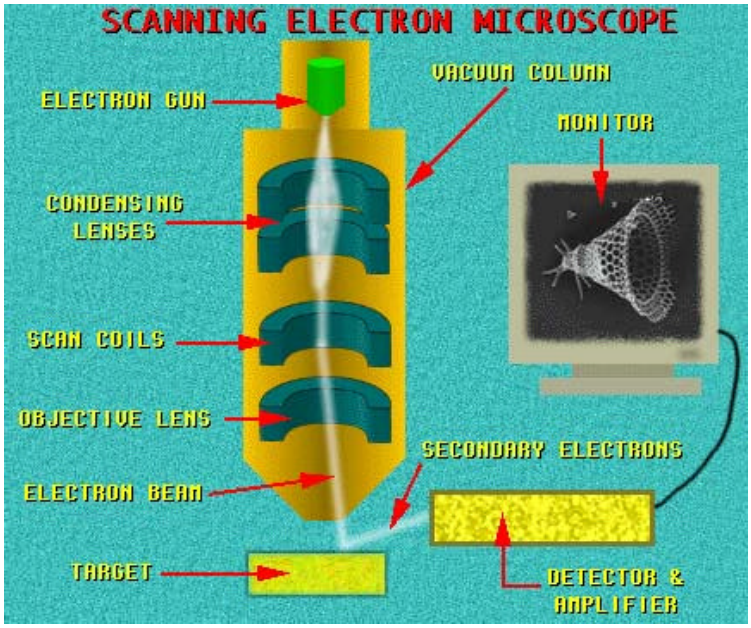


Figure 2.2 Scanning Electron Microscope flowchart [16]

Endotracheal tube cuff and tube samples, medical grade PVC pellets, and injection molded medical grade PVC were analyzed using SEM. Samples were mounted on SEM specimen holders using double-side carbon tape. Samples were then sputtered with either Au or AuPd using the VCR Group Incorporated D500i Dimpler. Three to seven samples were placed in the chamber, air was evacuated, and the samples were analyzed using the JOEL JSM-5910. Voltages between 2.5eV-13eV were used to view samples.

2.1.4 1-D Molecular Force Probe (MFP)-3. *Asylum Research, Inc* is a single axis force curve tracer. A flexible cantilever with a sharp probe tip deflects a near-IR laser beam in response to the forces between the cantilever tip and a sample. A piezoelectric translator (10um z-range) incrementally moves the tip towards the sample in the z-direction perpendicular to sample plane ("approach") and away from the sample ("retract") at a constant rate. The laser beam, focused no the backside of the end of the cantilever, is directed with a mirror into a split position-sensitive photodiode in order to give force detection and force range. This range is determined by choice of cantilever and can be

anywhere between 1pN and 1uN. The table below shows the values associated with various cantilevers. D, E and F cantilevers have IOLS and k values more appropriate for polymeric analysis. The MFP has been designed with an open fluid cell, so it can be used on a variety of polymeric or biological samples and in air or in fluids.

*(*courtesy of J. Cleveland, Asylum Research, Inc.)*

Lever	Type / Length	IOLS nm/V air/ water	quoted n_o (KHz) air	n_o (KHz) air/water	quoted k (N/m) air	measured k (N/m) air/water	Q air/ water	Force Noise in 1 kHz BW (pN) air/water
B	REC 200 µm	46.8/42	15	14.14/ 3.27	0.02	0.0243/0.02183	26.0/0.4	0.88/5.7
C	TRI 320 µm	77.65/ 61	7	6.127/ 1.021	0.01	0.01333/0.01263	16.4/0.5	1.1/6.3
D	TRI 220 µm	56.5/42.3	15	14.35/ 3.19	0.03	0.0425/0.0411	30.0/0.8	1.7/6.6
E	TRI 140 µm	40.2/27.8	38	31.93/ 7.84	0.1	0.1533/0.1352	45.3/0.9	3.8/8.1
F	TRI 85 µm	29.3/30.3	120	-/36.12	0.5	-/0.5965	-/2.2	15/12

IOLS =inverse optical lever sensitivity, n_o= resonance frequency, **k**=cantilever spring constant, **Q**=quality factor

The MFP was used in order to analyze and determine the adhesive forces on polymeric surfaces. Preliminary investigative testing of endotracheal tube surface forces was performed using Thermomicroscopic cantilevers in both air and PBS solution. Samples were attached to glass microscope slides using double-sided tape. The ***MFP-SA*** by Asylum, Inc., kept on top of a Halcyonics MOD-1 Active Vibration Isolation System in order to dampen the vibrations of the building and room, was used. Samples were tested in PBS solution in order to get an idea of how the surface forces can change in a saline-type environment. This testing was merely preliminary and intended to give experience in MFP

testing and supply a background in single-force microscopy from which more in-depth and specialized testing can be performed in the future.

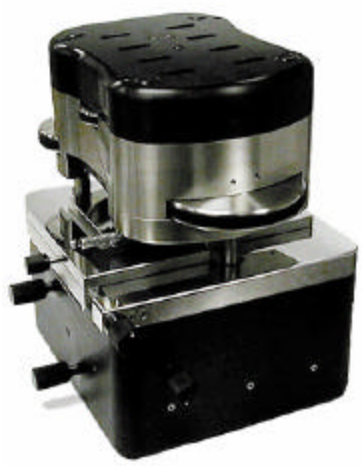


Figure 2.3 Picture of MFP-SA

2.1.5 Contact Angle Measurement is the measurement of the force balance between the liquid-vapor surface tension of a liquid drop and the interfacial tension between a solid and the drop. This is shown by the contact angle of a liquid drop of some specific solution (generally water) on the surface of a sample. By performing contact angle on a surface, unique insight into how the surface will interact with the external world can be gained. The droplet of liquid on the surface particularly gives insight on the hydrophobic/hydrophilic properties of a material surface. The basic relationship used in contact angle measurements which best describes the force balance is:

$$\gamma_{sv} = \gamma_{sl} + \gamma_{lv}\cos\theta$$

γ_{sv} = energy of the surface
γ_{sl} = interfacial tension between a solid and the drop
γ_{lv} = liquid-vapor surface tension
θ = contact angle Equation (1)

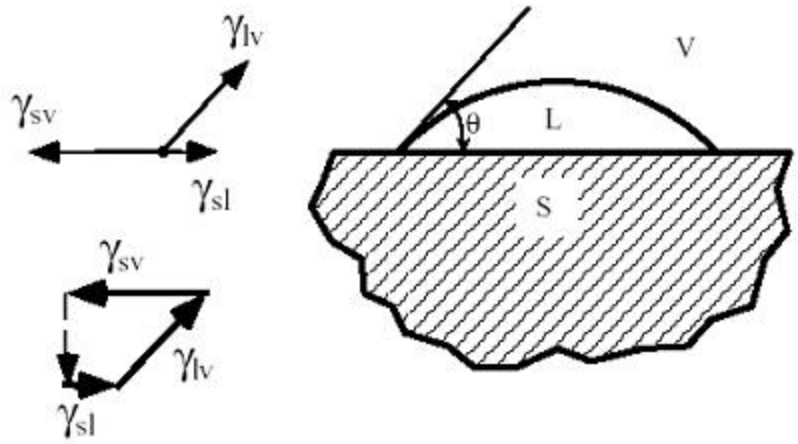


Figure 2.4 Contact angle measurement for a liquid drop on a solid surface and surrounded by a vapor [12]

Samples of endotracheal tube cuff, processed medical grade PVC and polyurethane samples were analyzed using contact angle measurements. Small droplets of ~0.5ml d-H_20 were put on samples which had been attached to glass slides using double-sided tape. The VCA2000 Video Contact Angle system was used to view and take pictures of the droplets on the polymer surfaces. Preliminary advancing and retracting methods of contact angle was used to observe the surface-water-air interface upon sudden addition of many small droplets and the interface upon putting a large droplet on the surface and removing the water from the surface at a constant rate. Pictures of various stages of the experiments were imaged using the video system.

2.2 Chemical Analysis

2.2.1 Fourier-transform infrared spectroscopy (FTIR) is an easy way to identify the presence of certain functional groups in a molecule. Additionally, FTIR can be used to confirm the identify of a pure compound or to detect the presence of specific impurities by the collection of absorption bands. In order to utilize an FTIR effectively, source energy

must be first sent through an interferometer onto the sample. This works by passing light through a beamsplitter, which sends light in two directions at right angles. These two separate beams pass travel different paths and then meet up again at the beamsplitter. Upon recombination, the difference in the path lengths create constructive and destructive interference called an interferogram. This recombined beam passes through the sample, which absorbs the different wavelengths characteristic of its spectrum. This subtracts specific wavelengths from the interferogram allowing the detector to report variation in energy versus time for all wave lengths simultaneously. The mathematical function called a Fourier transform allows the conversion of intensity versus time spectrum into an intensity versus frequency spectrum, useful for the identification of specific molecules.

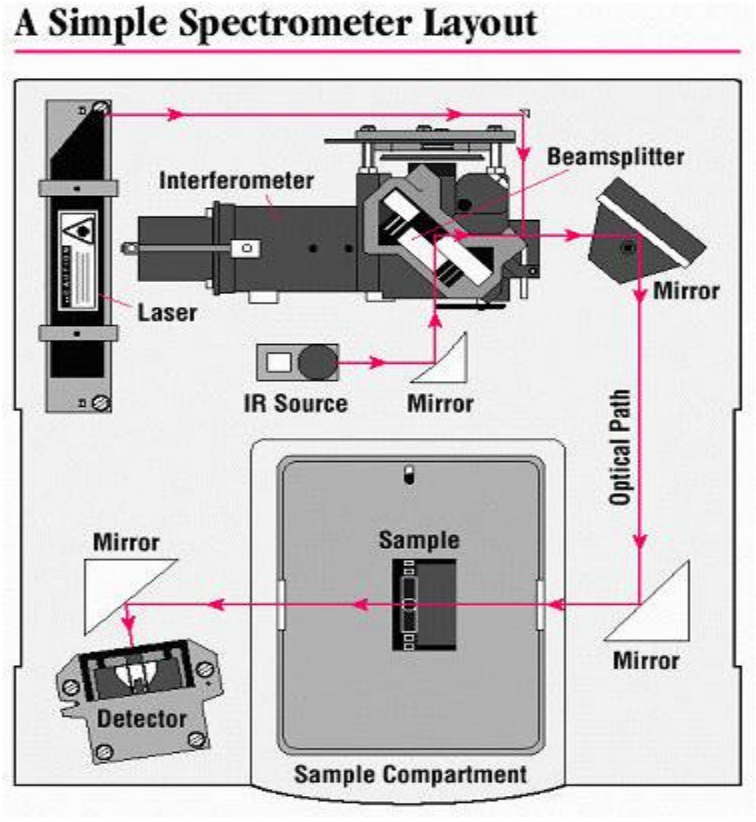


Figure 2.5 Schematic flowchart of FTIR

FTIR testing was completed on the endotracheal tube and cuff material to determine the general molecular components in the polymer. FTIR testing displays the resulting IR-spectrum and should correspond to the PVC and DEHP plasticizer spectra found in existing FTIR-spectrum libraries. This will also show if any unknown plasticizers are present in the PVC. The samples were tested using the Raman FTIR machine located in the CMSE Analysis Shared Experimental Facility, MIT Rm. 13-4139. The tube sample was placed on a glass slide and tested by reflecting the infrared rays off the sample. The cuff sample was sealed in a sample holder so the sample infrared rays could penetrate through the sample to give appropriate FTIR readouts on the attached computer.[5]

2.2.2 Differential Scanning Calorimetry (DSC) is an instrument used frequently to measure the thermal characteristics of materials. For every sample, heat flow in mW versus temperature was collected in the following manner. A sample of known mass is placed in a closed pan with a volume of 50 mL. This sample pan and an empty reference pan of the same volume are placed inside the DSC. As the temperature is raised at a steady rate, i.e. 5K/min, the DSC measures how much extra heat is put into the sample pan in order to maintain its temperature the same as the empty reference pan. The melting point of the material should be reached as the temperature is raised. The melting phase transition is an endothermic process and appears as a peak in the heat flow versus temperature plot, indicating that an added amount of heat is necessary to melt the sample (in comparison to the empty reference pan). DSC analysis determined the latent heats of melting and crystallization, which can be quantified from the area of the peak and dip in the heat flow versus temperature plot, respectively. Latent heat in Joules/gram calculated by dividing the area by heating rate x sample mass, shown in equation 2.

$$\frac{\text{area}}{\text{rate*mass}} = \frac{W*K}{\left(\frac{K}{s}\right)g} = \frac{J}{g}$$

Equation (2)

Differential Scanning Calorimetry testing from 0-300°C will be performed on small tube and cuff samples in order to observe the change in polymeric material as a function of temperature. At the DEHP flashpoint, approx. 215°C, a slight jump in the curve should be seen when the DEHP ignites and evaporates. This will aid in both characterizing the current tubes and cuffs, in addition to giving insight about the processing temperature range that should be utilized to combine DEHP and PVC. Tube and cuff samples, 35.5mg and 20.5mg, respectively will be weighed out and placed in small metal pans for use in the Perkin Elmer Pyris 1 Differential Scanning Calorimeter (DSC), located in CMSE's Analysis Shared Experimental Facility, MIT Rm. 13-4139.

2.2.3 Gel Permeation Chromatography (GPC) is a high performance liquid chromatography method by which number average weight, weight average weight and polydispersity of a polymeric material can be determined. For GPC work to be reproducible, it is necessary to have control over the following: flow rate, temperature and solvent composition. GPC involves the passage of a dilute polymer solution over a column of porous beads. High-molecular-weight polymers are excluded from the beads and eluted first. The lower molecular weight molecules pass through the pores of the beads, which increases their elution time. The effluent of the column is monitored as a function of time using an ultraviolet or refractive index detector. The amount of polymer eluted at set time intervals can be determined. The elution time of the polymer samples is compared with samples of known molecular weights giving an entire molecular weight distribution of the sample. From this, M_n and M_w can be determined for each specific sample.[26]

Gel permeation chromatography was used on the commercial endotracheal tubes to determine the molecular weight of the PVC. Both samples were prepared in 10ml of THF to a concentration of 0.5%g/v, and the solutions placed in a 45°C compartment overnight. After solubilizing overnight at 45°C, the endotracheal tube sample solution was clear, but there was a fine, white sediment at the bottom of the vial. The solute portion only was pipetted into a filter syringe, and filtered easily. The PVC pellet solution was clear, and filtered easily. The instrumentation used was the Waters Alliance GPC2000 which ran the samples at 1ml/min in THF solvent @45°C/RI detector. The Polymer Labs columns used were guard + 2 mixed bed C's & 100A, and the calibration PS standards ranged from 2.4x10E6 to 266 daltons. All testing was performed at the Glidden/ICI Paints Strongsville Research Center in Ohio.

2.2.4 Accelerated Solvent Extraction (ASE) is an automated system for separating composite materials by a means of extracting out a chosen material from the sample. This method can be used to extract plasticizer from PVC, allowing for further analysis of weight percent plasticizer and GC testing of plasticizer to determine the specific molecular structure. Samples are placed in an extraction tube and heated at high temperature and pressure. Often pressures are greater than 1000psi and temperatures rise above the normal boiling point. ASE has the ability to complete the extraction process in less than 20 minutes with final volume samples less than 50ml. Once solvent is extracted, the resulting extract is transferred to successive 60 ml vials for further concentration and analysis.

This relatively new procedure greatly minimizes the waste produced. It also minimizes the time needed. The alternative, soxhlet extraction, is performed by a distillation process where solvent amounts greater than 300ml may be needed and anywhere

from 12-76 hours are necessary for complete extraction to occur in a sample.

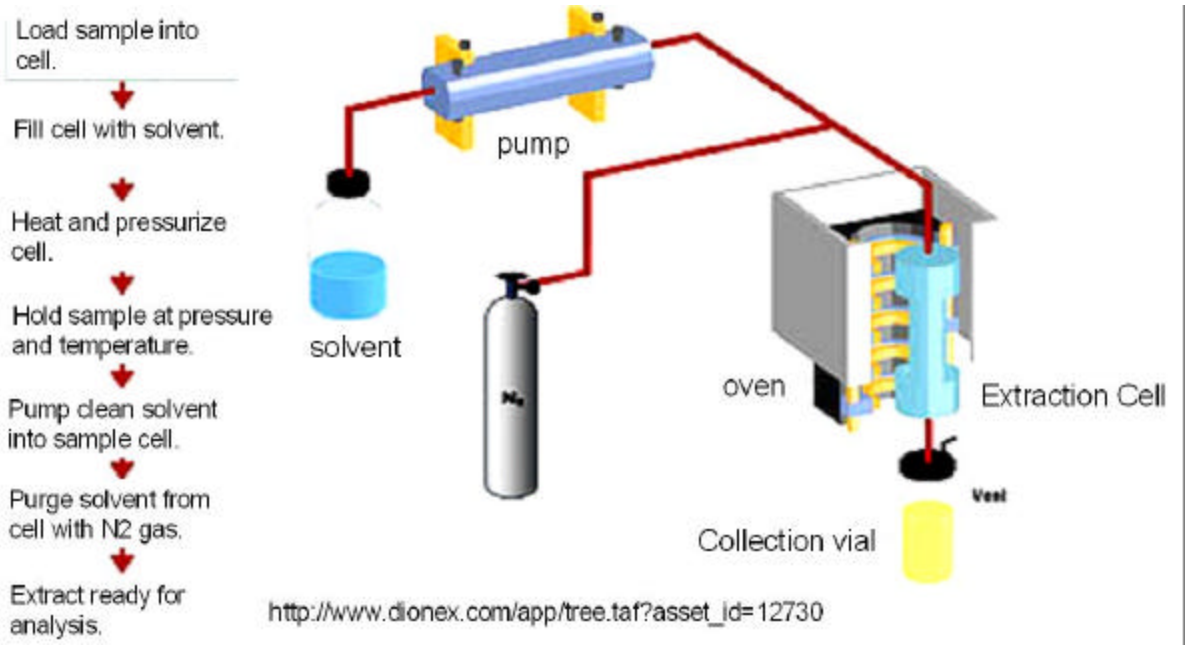


Figure 2.6 Diagram of the solvent extraction pathway used in the ASE200

Endotracheal tube and medical grade PVC pellets were analyzed using the ASE 200 at the Dionex Corporation located in Salt Lake City, Utah. Samples were cryogenically ground using the Cryograinder SPEX CertiPrep 6750 which uses liquid N_2 to cool the sample, allowing magnetic forces to crush the polymer as the machine rapidly shakes the sample. Approximately 0.5g of each ground sample was put in an 11ml sample cell, the oven temperature was set to 100°C, pressure to 1500psi and the extraction time set to 14 minutes. During the testing, each sample was flushed with petroleum ether four separate times in order to extract the maximum amount of plasticizer located in the sample. Once elutions were obtained, excess petroleum ether was evaporated off under a hood, leaving pure plasticizer that was ready to be prepared for Gas Chromatography (GC) analysis.

2.2.5 Gas Chromatography (GC) is, more specifically, gas-liquid chromatography. GC requires that a sample be dissolved in a solvent, generally a more toxic solvent, such as

methylene chloride. A sample is vaporized and injected into a chromatographic column. The sample is transported through the column by gaseous flow. A graph is produced which shows the mV versus time measurements for samples, detecting larger and smaller mass locations. From the charts, the particular sample type can be identified.

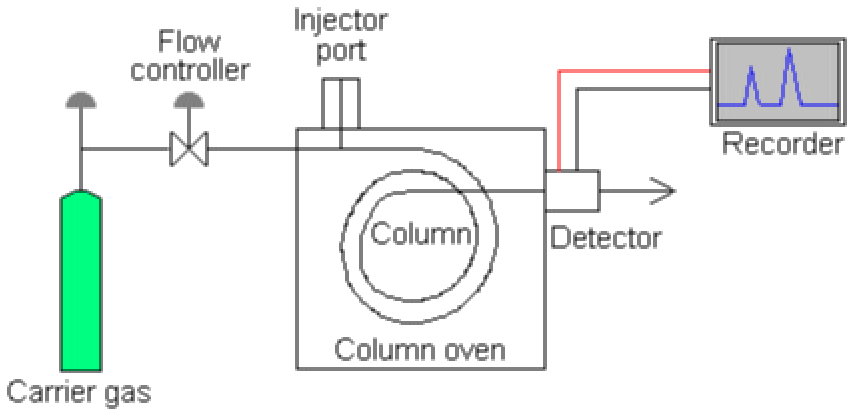


Figure 2.7 Schematic diagram of sample flow through a GC [17]

GC analysis was performed with the assistance of staff at Dionex Corporation. An HP 6890 Series GC System was used for experimentation. Plasticizer extractions from ASE were diluted with methylene chloride in small vials optimal for GC testing. Once samples were injected and parameters were set, the machine pumped gas through the chamber, injected small samples of each material, and gave area mV versus time output graphs. These graphs were analyzed and the specific plasticizers were determined. The following parameters were used for GC testing:

df = 0.25um
flow rate = 3.0ml/min constant flow
Oven = 210(1)-10-315(1)
Injection Temp. = 325C
Detection Temp. (FID) = 350C
split ratio = 25:1

2.3 Mechanical Analysis

2.3.1 Uniaxial tensile testing is a method commonly used to identify mechanical properties of materials. Tensile testing can be used to obtain information to gain either stress-strain or load-elongation graphs of a sample. Test specimens are generally made in a dogbone shape (shown in Figure 2.8), clamped into tensile grips, and is gradually elongated, at a specified rate, parallel to its longitudinal axis. The imposed load is the uniaxial tension. The load necessary to deform the specimen is recorded simultaneously as a function of time. The load or displacement values can be plotted versus time or against each other. Typically, the graph obtained is altered by dividing the load by the initial specimen cross section to obtain the stress, and to the elongation is described as a percentage in order to make the typical stress-strain curve. This curve can give information about the sample, such as tensile modulus, fracture stress and strain, plastic deformation and elastic deformation in the material.

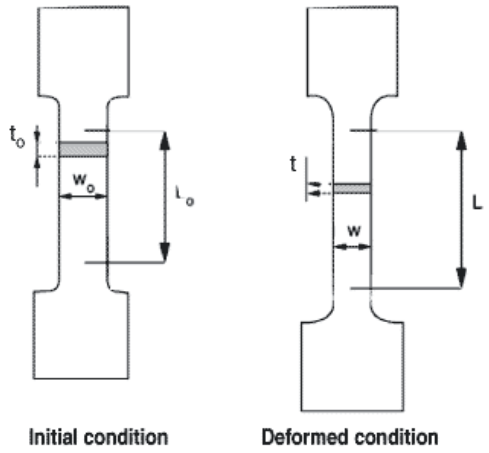


Figure 2.8 Dogbone specimens under initial and deformed conditions [15]

Uniaxial tensile testing was performed using a TEE32 Texture Analyzer with a 30kg load cell. Tube and cuff samples of 22x3x1.5mm and 22x3x.03mm dog bone shaped specimens were cut from endotracheal tubes and cuffs, respectively. Dogbone specimen of

similar proportion were formed using processed medical grade PVC and also analyzed using the texture analyzer. The tests give deformation vs. time graphs, which allows simple mathematical manipulation to create the stress vs. strain curves. These curves give information about the polymeric structure of the PVC, including yield strength, strain softening, fracture strength, extensibility and the Young's Modulus. The TEE32 Texture Analyzer used is shown in Figure 2.9

Figure 2.9 Picture of TEE32 Texture Analyzer used during for uniaxial analysis.

2.3.2 Injection Molding is a processing method which can be used to mold plastics whose processing temperature (glass and melting temperatures) are too high to work with in an ordinary chemical laboratory. The mini-jector injection molding machine is a single screw injection molder. Pellets of polymer are placed in a hopper, which feeds pellets into the machine as necessary. The machine is heated to the desired temperature necessary for melting the plastic, hydraulic pumps are used as the means to raise the injection plunger up in order to allow pellets to fill the screw area. The screw mixes/melts the polymeric material, and, before molding, the machine must be flushed of old polymeric material that may be left in the screw injector. About 1/3-1/2 kg of material must be flush through the machine, injected into a waste holder, and thrown away. Once the material appears to be solely made of the desired polymer, a v-shaped mold can be inserted into the machine. The

polymer is then injected into the mold that has been inserted in the base of the machine. This is shown in Figure 2.10. A mold injector bar is used to release the v-shaped mold from the machine. The mold can then be opened and the desired plastic sample can be removed from the machine. Multiple samples can be molded using the same mold and set up, and without having to flush the system again.

A mini-jector injection molding machine was used to process medical grade PVC of varying durometers, i.e. varying concentrations of DEHP. Molds of tensile testing dog bone-shaped specimen and thin films will be processed for testing and analysis. This method will utilize a large (1-2kg) amount of medical grade PVC. The Mini-Jector 55, which is a single screw injection device, is located in the basement of the MIT Media Lab. By doing this, the hope is to create standardized samples that can be tested and whose results can be compared with the results from commercial endotracheal tubes. [2]

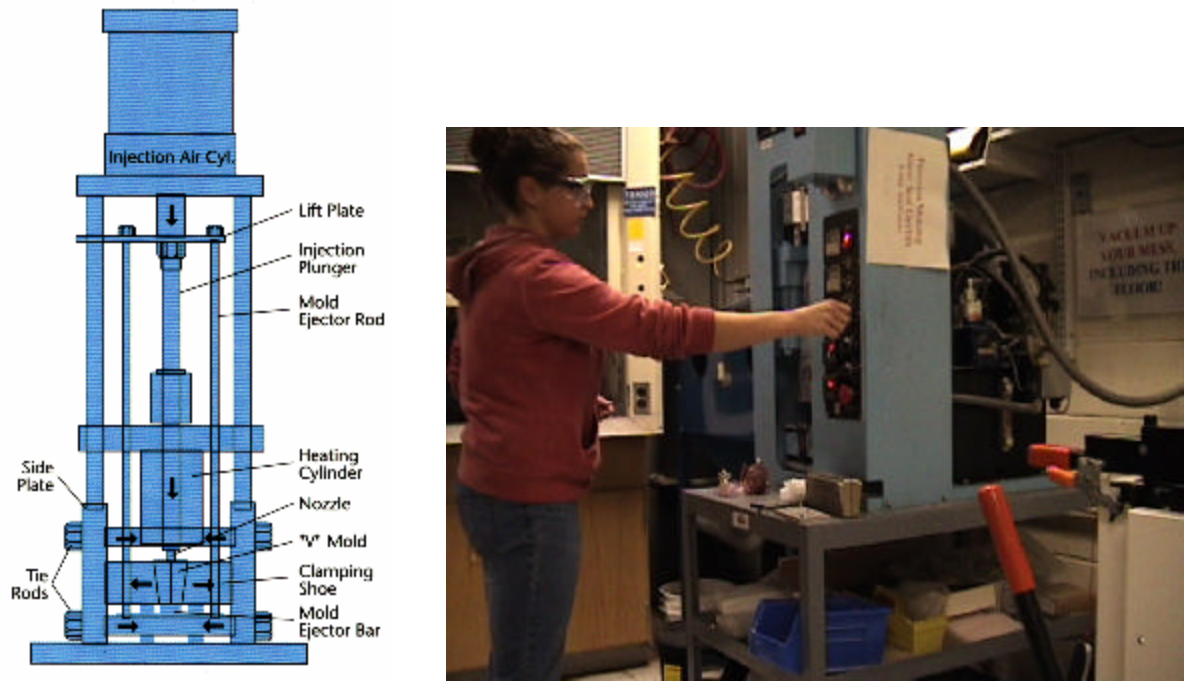


Figure 2.10 **(a)** Schematic of a single-screw injection molding machine
(b) Picture of injection molding using the Mini-Jector located at MIT

2.3.3 Cuff Herniation Testing is a ASTM requirement for endotracheal tube standardization. The endotracheal tube cuff area must be inflated until firm, the diameter measured on all sides, then the apparatus is left sitting overnight to observe any cuff herniation that may occur during that time. Figure 2.11 shows the simple apparatus built in order to firmly hold the ET, inflate the cuff, and relatively accurately measure the diameter of the ET.

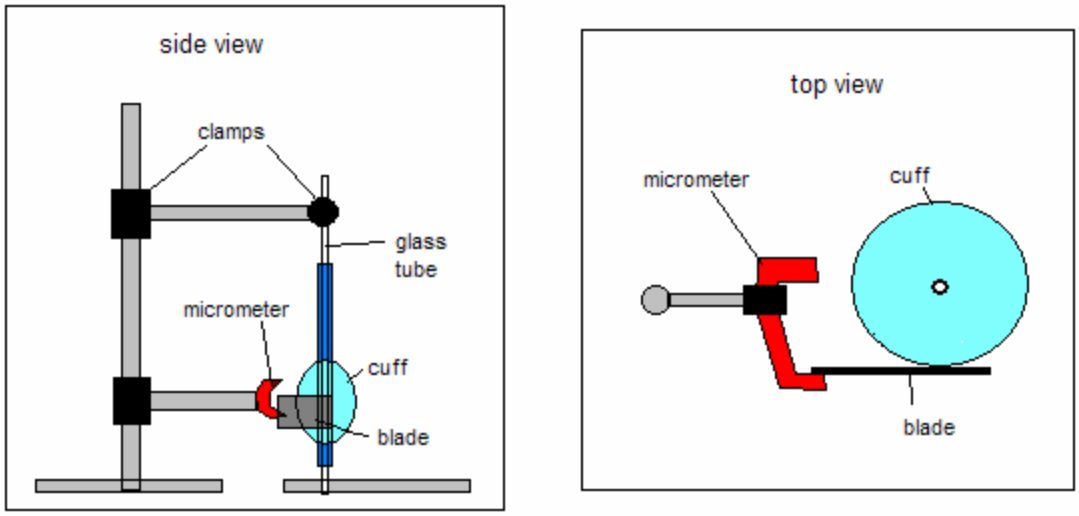


Figure 2.11 Schematic of apparatus built to perform cuff herniation testing

A Mallinckrodt Endotrol endotracheal tube was clamped into the apparatus above and inflated with 35ml of air, measured, inflated to 60ml, measured, left overnight, then measured again for any noticeable herniation of the ET cuff.

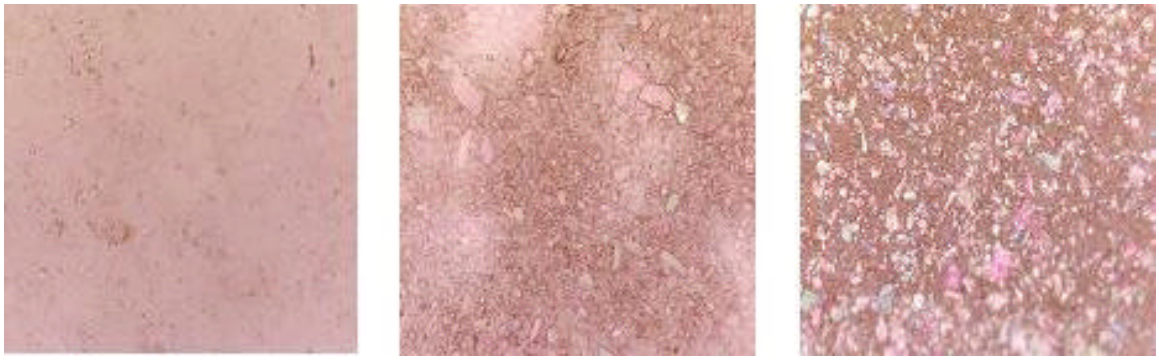
3 RESULTS AND DISCUSSION

3.1 Microscopic Analysis Results

3.1.1 Optical Microscopy

Figure 3.1 presents representative images taken using an optical microscope at 50x magnification of ET cuff and tube samples and give insight into the microscopic surface

features of ETs. As-received, unaltered cuff samples, shown in Figure 3.1 (b), showed small colorful crystals on the sample surface approximately 0.5-1.5 μm in size. To further investigate the nature of these crystals, a number of surface treatments were employed. Figure 3.1 (a) shows a sample which has been wiped with Kimwipes (made from 100% virgin wood fiber) in an effort to mechanically remove surfaces particles, crystals, or other debris. This image shows no reflecting areas and suggests that the crystalline areas seen in the unaltered sample may, indeed have been plasticizer. Further testing was performed using petroleum ether (PetEther) as a means to leach out plasticizer from the sample, since the plasticizer is soluble in the PetEther while PVC is not. It was observed that even though the PetEther dissolves plasticizer while leaving PVC in tact, it evaporates so quickly that it is then redeposited (recrysallized) on the surface. Figure 3.1 (c) gives strong evidence that PetEther did leach plasticizer, which then recrystallized on the surface of the cuff leaving the highly reflective surface shown in (c).



(a) (b) (c)

Figure 3.1 Optical images of Endotrol Cuff

(a) Wiped off surface

(b) Unaltered surface

(c) 1 hour soak in Petroleum Ether

3.1.2 Atomic Force Microscopy

AFM images were taken of endotracheal tube samples giving images such as those shown below in Figures 3.2-3.4. The images taken were 5x5 *u*m areas of endotracheal tube. The shown images are deflection images, which give a clearer view of the surface features than a height image. While the color gradient scaling is not accurate in a deflection image, the following images give an overall impression of the nanoscopic surface features of an ET cuff sample. These images, taken in air, show a range of surface features depending on the alteration of the surface. The unaltered cuff surface shows areas with crystals which appear to completely cover the surface area. The rinsed and wiped sample (Figure 3.3) does not appear to have large crystalline areas on the surface, but instead, appears much flatter than the other samples and has a surface covered with small waves. The surface which was altered by rinsing with Petroleum Ether displays areas which look similar to the crystalline areas of the unaltered surface and patches which appear to have small, bumpy areas like those seen in the rinsed and wiped sample.

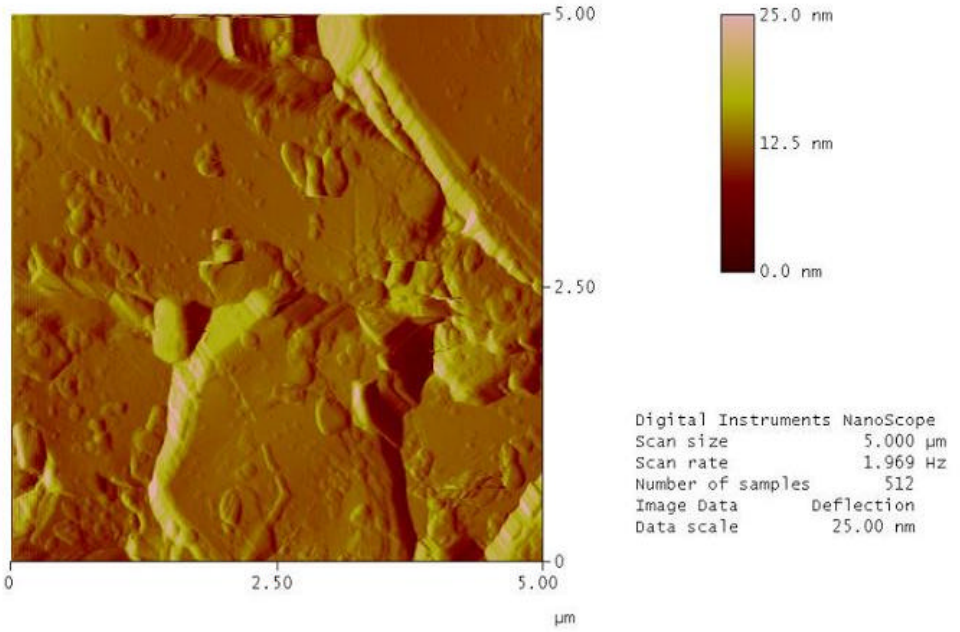


Figure 3.2 Deflection image of unaltered ET cuff surface

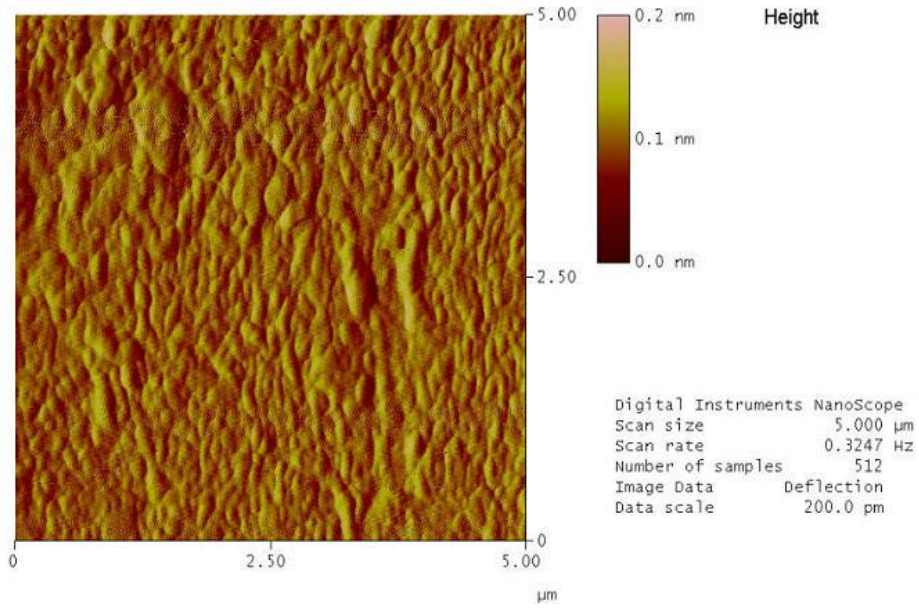


Figure 3.3 Rinsed and wiped surface of ET cuff surface

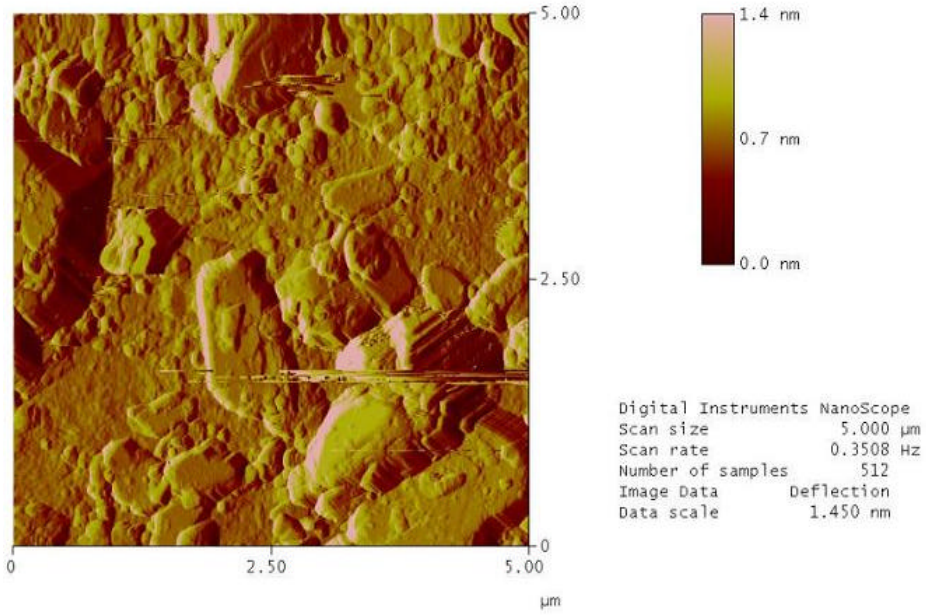


Figure 3.4 Image of ET cuff surface after 24 hr. PetEther rinse

Further analysis of the height variance between samples is necessary to make better judgement between the unaltered and petroleum ether rinsed ET cuff samples. Preliminary investigation has occurred, but adequate results have not yet been obtained. The primary reason for the inadequacy of the results is the difficulty in maintaining tip contact with the

surface when doing height imaging. The cantilever has a high tendency to get stuck in grooves between crystals, which causes the AFM to lose contact with the surface and make the scan insufficient for proper analysis.

3.1.3 Scanning Electron Microscopy

SEM results agree with the AFM results because the results for an unaltered cuff surface also show a surface scattered with crystalline areas. An image taken at 5eV showing a x1,800 magnification of the cuff surface is shown in Figure 3.5. This image gives additional insight to the size and variety of the crystals which lie on the surface. Unlike the AFM image, the SEM image can easily vary the dimensions of the area under analysis and in far less time.

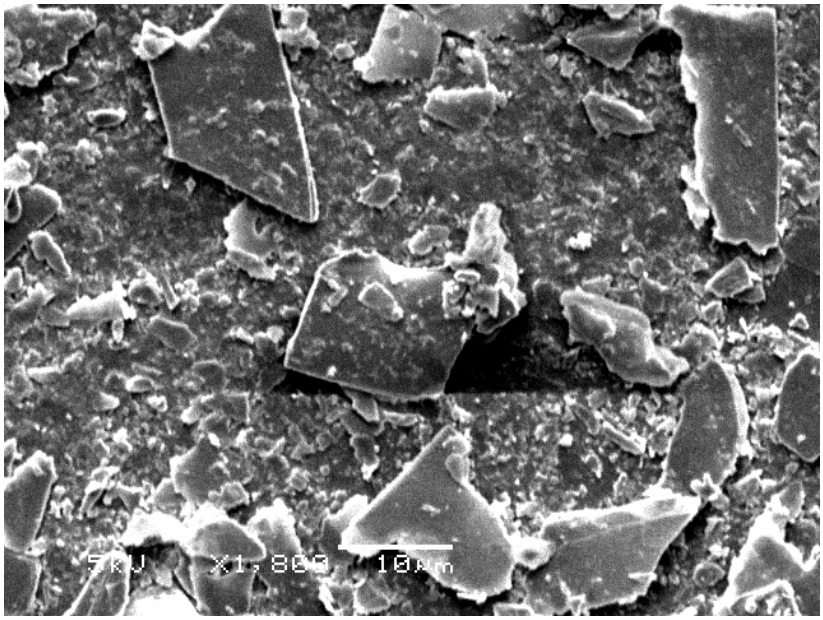


Figure 3.5 Unaltered ET cuff at x1800 magnification

Images have been taken of a cut surface of Endotrol tube as well to observe any plasticizer that may also lie on that surface. From images taken, shown in Figure 3.6, small crystalline areas, similar to those observed on cuff samples can also be seen. This implies that, yes, the crystalline areas seen are plasticizer which has leached from the PVC matrix.

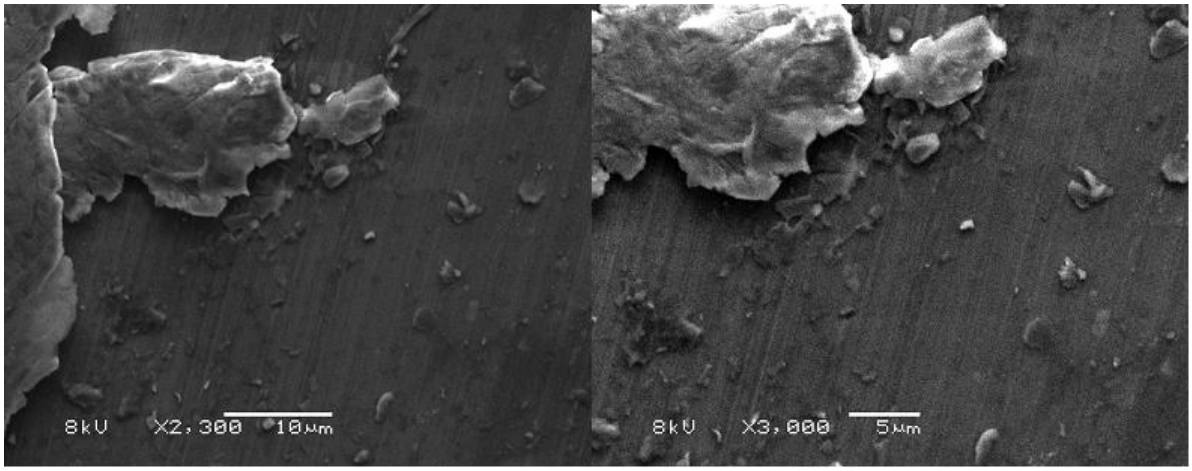


Figure 3.6 Images of endotracheal tubing at x2300 and x3000 magnification

In addition to viewing surface areas of tube and cuff samples, samples of ET cuff have been observed from the side in order to accurately determine the thickness of the Mallinckrodt Endotrol Endotracheal Tube under analysis. From the images, it appears that the cuff thickness is approximately 40 microns, which is helpful in mechanical testing and analysis of cuff properties. Plasticizer also appears to lie on the edges of our cuff samples as well, which can be seen in the image below.

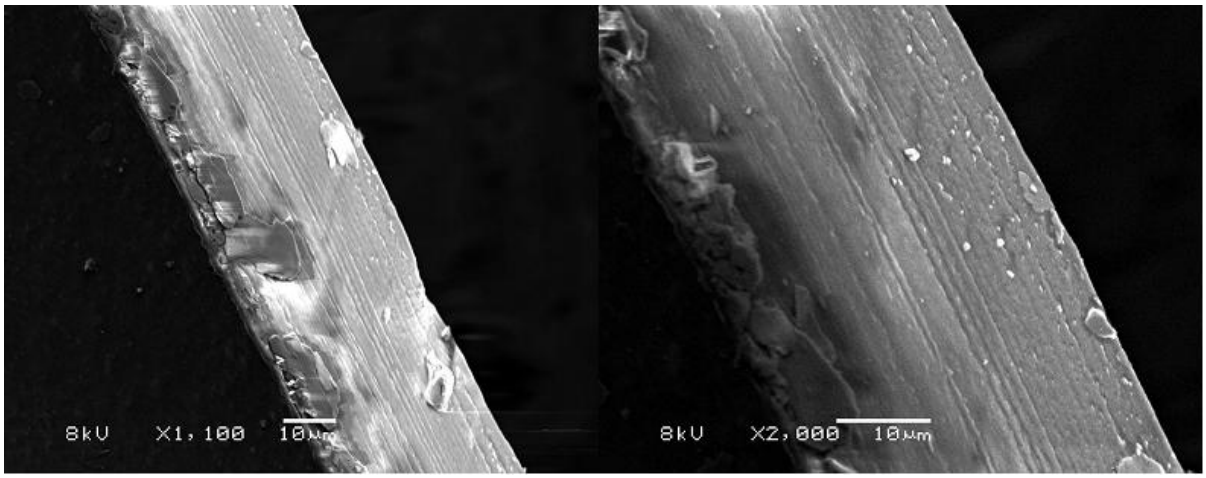


Figure 3.7 Images of the edge of an ET cuff sample at x1100 and x2000

3.1.4 1-D Microscopic Force Probe

Table 3.1 and the following histograms compare the MFP total adhesive force curves of Endotrol cuff samples using a Si_3N_4 probe tip in both air and PBS solution using three different thermomicroscope cantilevers. D and E cantilevers were used, which have spring constants of 0.03 N/m and 0.1 N/m, respectively.

Table 3.1 Thermomicroscope Tip D and E in Air and PBS Solution

	Total Pulls	# pulls, % found in best peak	Range of Peak (nN)	Pulls, % found in second best peak	Range of Peak 2 (nN)	Best Average Adhesive Force
Tip D in Air	51	34 pulls, 67%	18.8-20.4	NA	NA	19.6 nN
Tip E in Air	44	29 pulls, 66%	18.78-20.32	NA	NA	19.66 nN
Tip D in PBS	48	34 pulls, 70%	0.54-1.04	NA	NA	0.8 nN
Tip E in PBS	63	36 pulls, 57%	0.83-1.11	20 pulls, 32%	0.31-0.55	0.95 & 1.1 nN

The following histograms diagram the range of adhesive forces which may be gained during MFP testing. Further analysis must be performed using an MFP 3-D in order to observe exactly what the surface features look like at various locations along samples. During 1-D testing, it is impossible to know exactly where and what the cantilever is hitting on the surface. Future analysis of the adhesive surface forces may also give insight into tissue-polymer relations of PVC/plasticizer and endotracheal tissue. These preliminary results are encouraging, however. Despite the use of varying cantilevers, the overall force results were similar for tests in air and PBS solution.

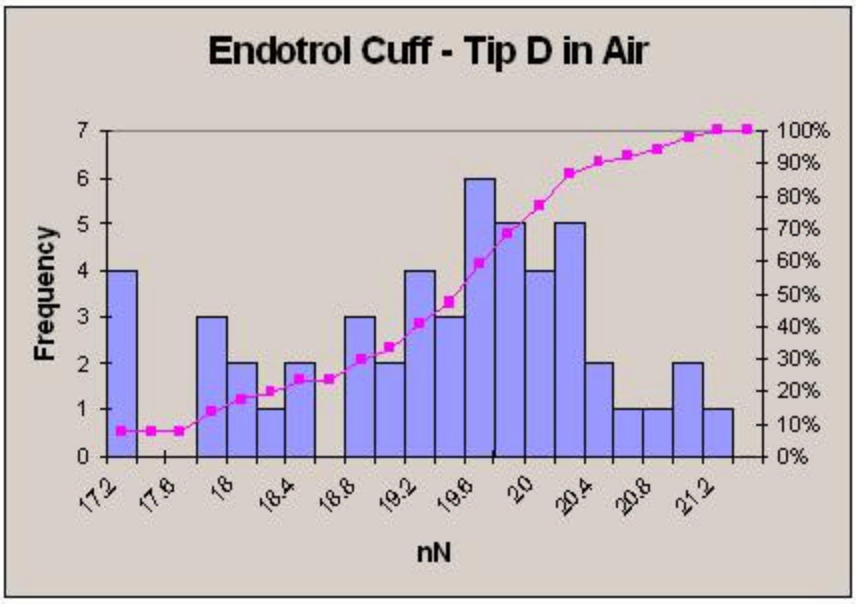


Figure 3.8 Histogram of the adhesive force (nN) of cuff using D cantilever in air.

The cantilever used had an IOLS = 70.03nm/V, K= 41.3pN/nm (k = 0.037N/m), and Resonant Frequency = 14,682.

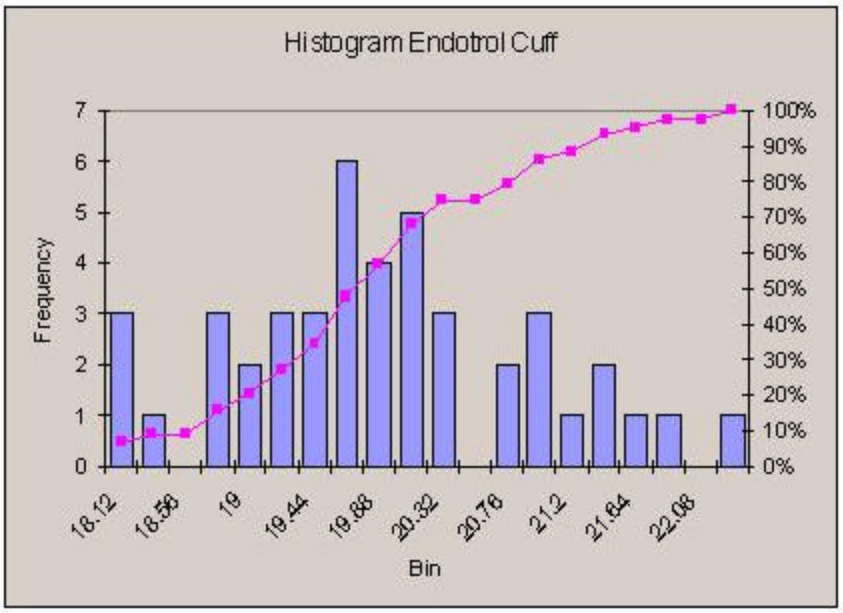


Figure 3.9 Histogram of the adhesive force (nN) of cuff using E cantilever in air.

The cantilever used had an IOLS = 36.34nm/V, K= 148.1pN/nm (k = 0.14N/m), and Resonant Frequency = 32,768.

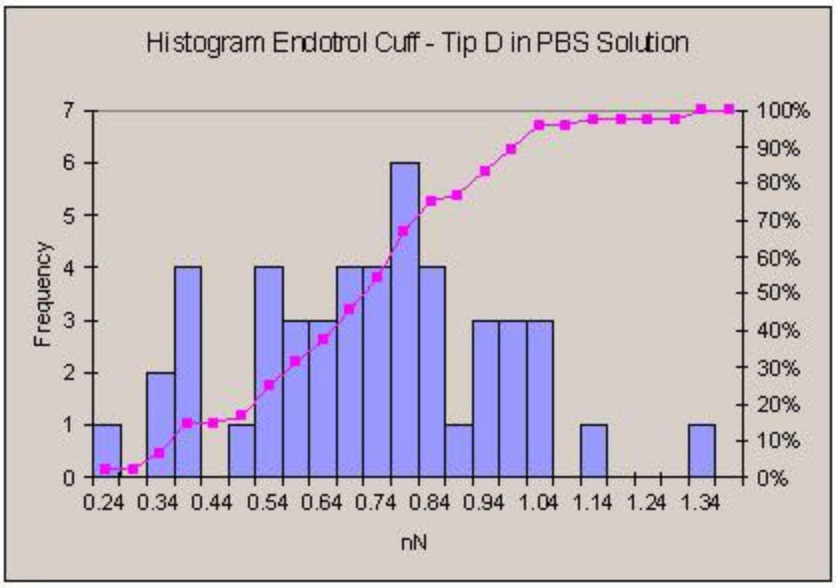


Figure 3.10 Histogram of the adhesive force (nN) of cuff using D cantilever in PBS. The cantilever used had an IOLS = 42.17nm/V, K= 33.0pN/nm (k = 0.038N/m), and Resonant Frequency = 3,190.

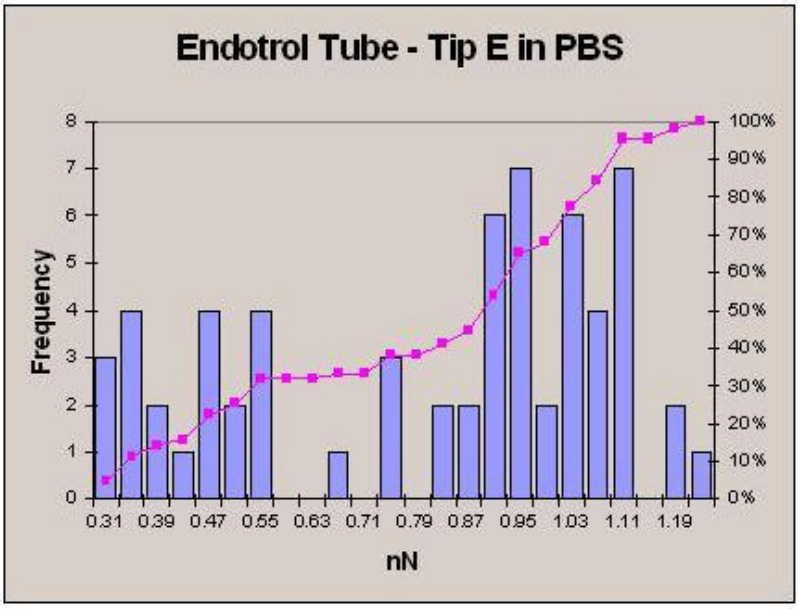


Figure 3.11 Histogram of the adhesive force (nN) of cuff using E cantilever in PBS. The cantilever used had an IOLS = 40.94nm/V, K= 163.0pN/nm, and Resonant Frequency = 67,654.

3.1.5 Contact Angle Measurements

Approaching and receding contact angle measurements were performed on unaltered endotracheal tube cuff samples. For approach testing, an initial and final image was taken of the droplets on the surface of the samples. The hydrophobic properties of unaltered cuff were noticeable from the approach testing. Figures 3.12 thru 3.15 display the initial and final images of droplets before and after rapid addition of water (advancing) and before and after the removal of water (receding).

Figure 3.12 Initial image of small water droplet before addition of water on ET cuff surface

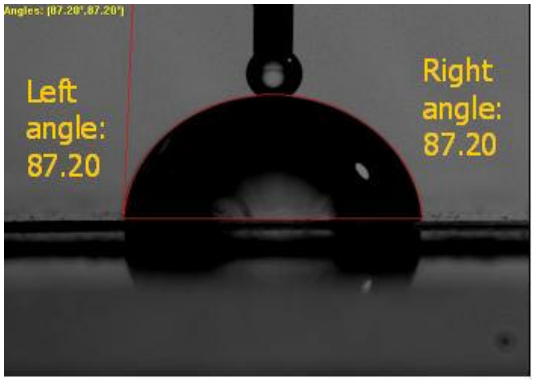


Figure 3.13 Final image of advancing water droplets on ET cuff surface

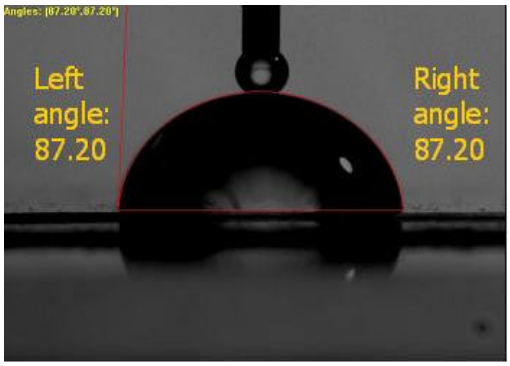


Figure 3.14 Initial image of water droplet on ET cuff surface before receding

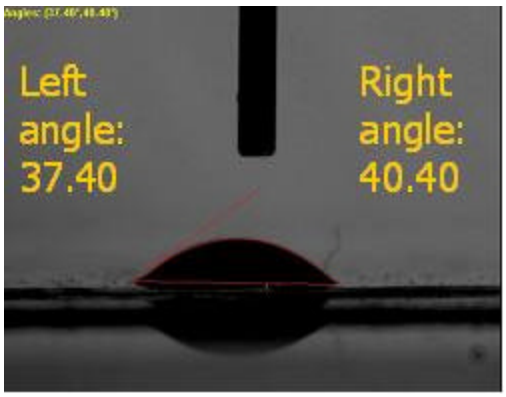


Figure 3.15 Final image of receding water droplet on surface of ET cuff

Overall, it appears that an unaltered cuff surface has relatively high hydrophobic properties. By applying advancing and receding water droplets to the ET surface, observations about the surface-liquid-air interface can quickly be made. Contact angle measurements varied from 81.5° +/- 6.5° for the majority of the contact angle measurements. From these generalized tests, future research can be performed in which modifications can be made to the surface which may affect the hydrophobic properties of ETs. Ideally, tubing will be made more hydrophilic, hence, attracting water molecules rather than cells and proteins which then attract bacteria that adheres to the tubes.

3.2 Chemical Analysis Results

3.2.1 Fourier-transform infrared spectroscopy

The FTIR results of cuff and tube testing are shown in the graph below. The graph shows a reading of wavenumbers vs. absorbance, which, in turn gives information about the molecular structures of the endotracheal cuff and tube material tested. Peaks on the graph have been labeled according to the molecular structure that is identified by an associated wavenumber. From the results, C-H bonds, and weak C-H bonds on benzene rings are seen around 3000cm^{-1}. Ester linkages are shown at 1715cm^{-1}, a benzene ring appears present around 1470cm^{-1}, C-C bonds around 1350cm^{-1} and C-O bonds around 1200cm^{-1}. From these results, esters, benzene rings and C-O bonds were observed, supporting the existence of plasticizer on the surface of the ET tube and throughout the ET cuff samples measured.

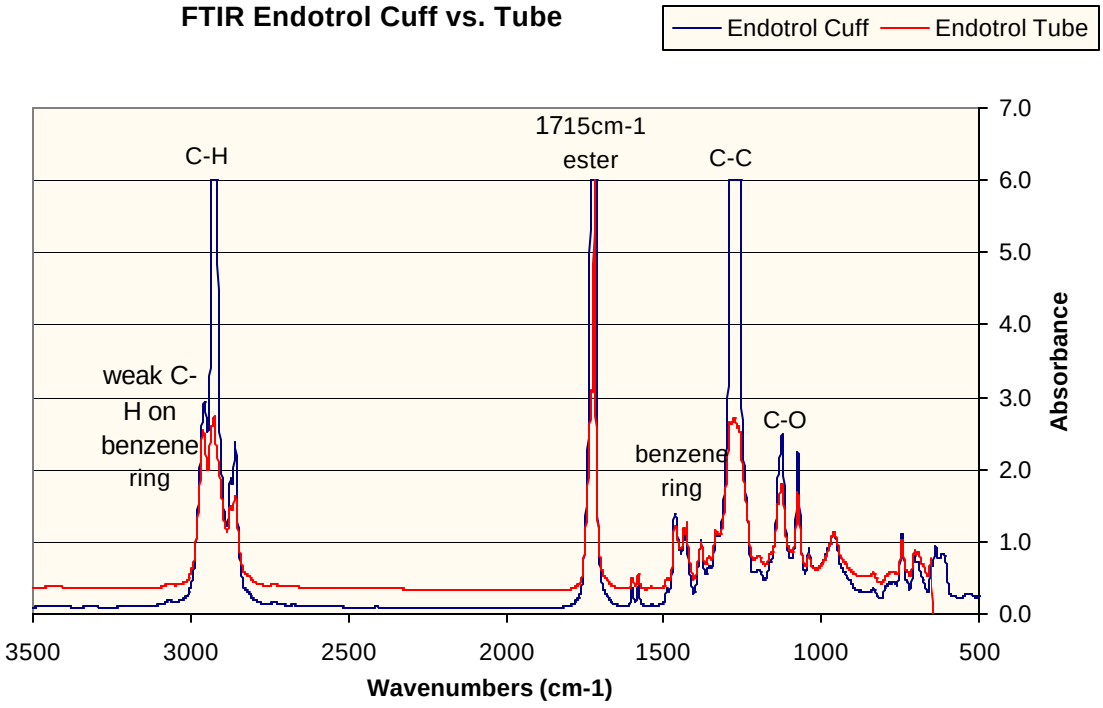
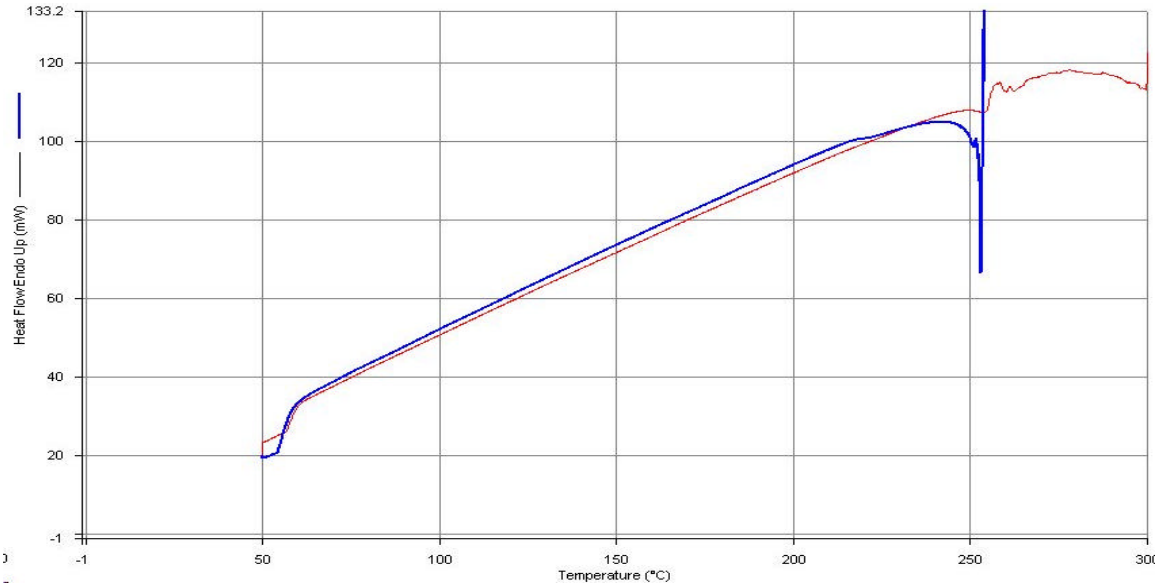


Figure 3.16 FTIR results from a Mallinckrodt Endotrol cuff and tube sample

3.2.2 Differential Scanning Calorimetry

The graph shown in Figure 3.17 compared samples of endotracheal tube cuff and tube fragments as the temperature rose from 50-300°C at a rate of 10°C per minute. There appears to be a change in both samples around 60°C and a slight change again near 220°C. The sample appears to have a glass transition temperature, Tg, at about 60°C. The flashpoint for the DEHP plasticizer is expected to be 207°C (405°F), hence, the slight fluctuation seen in heat flow as temperature increased gives reason to believe that the alteration was the combustion of plasticizer. The samples should exhibit the same properties because they are both composed of the same MW, shown through ASE and GEC results. Optical microscopy images showed large voids throughout the polymer, which suggests the flashpoint of DEHP plasticizer was reached. The DSC analysis gives information with regards to the temperature at which PVC/plasticizer can be processed so as not to rise above the point at which degradation will occur.

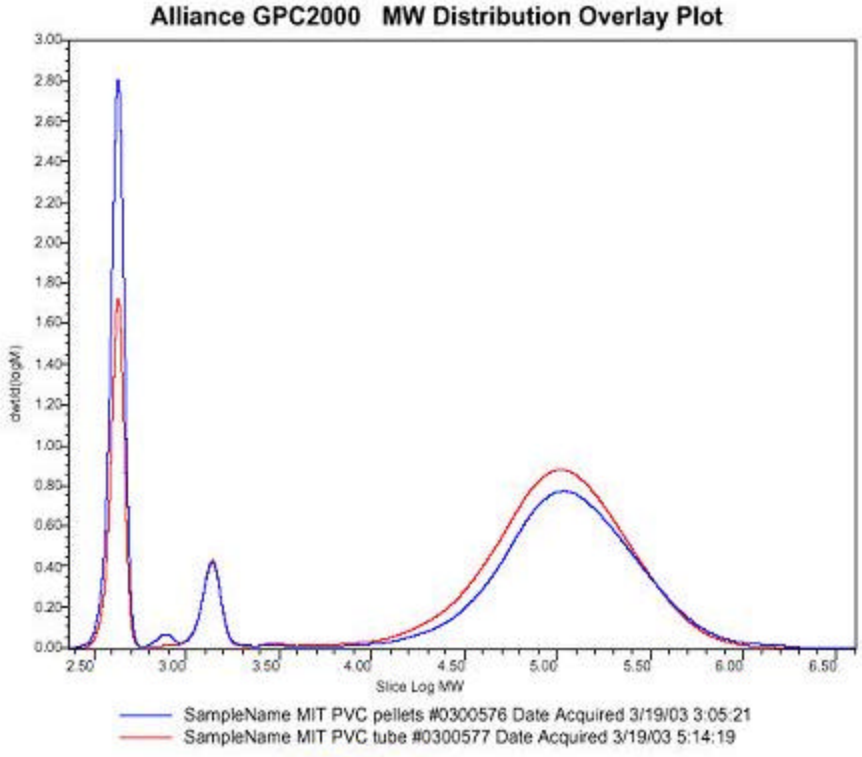


* Blue = 35.5mg tube Red = 20.5mg cuff

Figure 3.17 Heat Flow (mW) vs. Temperature (C°) of Mallinckrodt Endotrol tube and cuff samples.

3.2.3 Gel Permeation Chromatography

Figure 3.18 is an overlay of the molecular weight distribustion's of PVC/plasticizer in endotracheal tubes and in similar medical grade PVC. One feature of the plot is the difference between the samples in the amount of the ~400dalton component. Another difference is the near absence of the peak at ~770daltons for the Endotracheal tube material compared to the pellet material. These low MW peaks may be plasticizers or some other additives. Included in this report are two individual reports that highlight each peak (Mp) in the distributions and give its relative % Area of Integration.



GPC Results

	SampleName	Mn	Mw	MP	Mz	Mz+1	Polydispersity
1	MIT PVC pellets #0300576	8493	111786	427	355571	746227	74.886379
2	MIT PVC tube #0300577	2360	112334	427	278436	521191	47.601069

Figure 3.18 GPC overlay plot showing the molecular weight of ETs & PVC pellets

From the GPC testing, the molecular weight (MW) of Mallinckrodt Endotrol endotracheal tubes has an average value of 111,786 g/mol. The MW of PVC pellet has an average value of 112,334g/mol. The polydispersity index's (PDI) were quite large, 74.89 and 47.60 for tube and pellet, respectively. The high PDI indicates a relatively large breadth of molecular weight distribution. Despite the high PDI, the overall molecular weight properties of the poly (vinyl chloride) can be gained from GPC analysis.

3.2.4 Accelerated Solvent Extraction

ASE testing was performed in order to determine the weight percent of plasticizer in endotracheal tubes. The testing successfully removed all plasticizer from PVC. The test was performed on a Mallinckrodt Endotrol endotracheal tube and also performed on a mix of 70-77 durometer PVC pellets. The durometer refers to the flexibility, or amount of plasticizer in the polymer. From the extraction, it was determined that the Endotrol tube was composed of ~63.40% pure PVC and ~36.60% plasticizer. The PVC pellets were composed of ~61.27% pure PVC and ~38.73% plasticizer. The results determined from testing are significantly faster and are more accurate, having a 100.7-102.6% recovery over Soxhlet extraction, according to the workers at Dionex Corporation.

3.2.5 Gas Chromatography

Gas chromatography results were gained to determine the exact type of plasticizer in the PVC pellets and endotracheal tubes. A run was performed using plasticizer standards of di-octyl adipate (DOA), tri-octyl phosphate (TOP), di-octyl phthalate (DOP) (same as DEHP), and tri-octyl tri-mellitate (TOTM). These gave appropriate time at which to expect to see common PVC plasticizers during GC testing. The GC readings showed both samples only containing one type of plasticizer, which was DOP (DEHP). The Endotrol tube

reading was 4.614 minutes, and the PVC pellets were at 4.567. The resulting peaks lay within +/- 0.03 minutes from the standardized DOP reading, which was 5.585 minutes. These results are important, because they state explicitly the type of plasticizer used in this particular, common brand of endotracheal tubes.

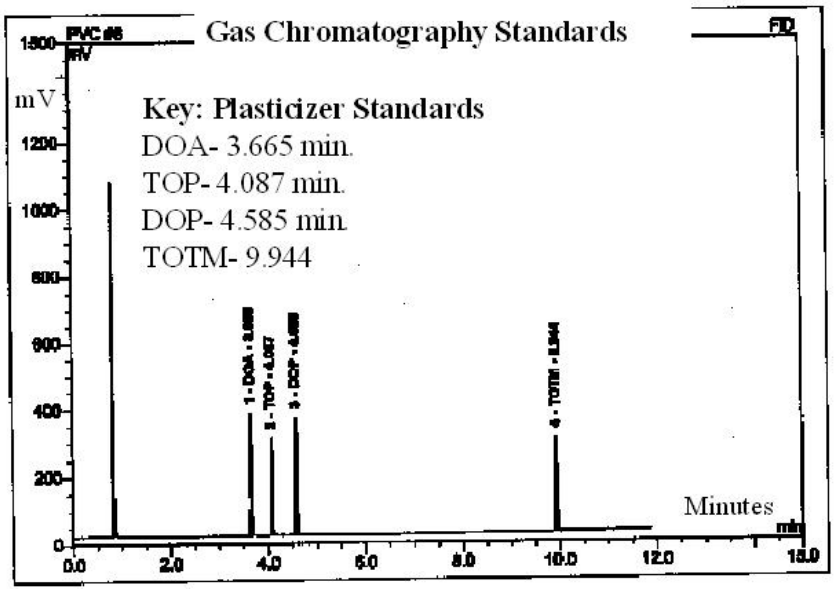


Figure 3.19 Gas Chromatography results for plasticizer standards

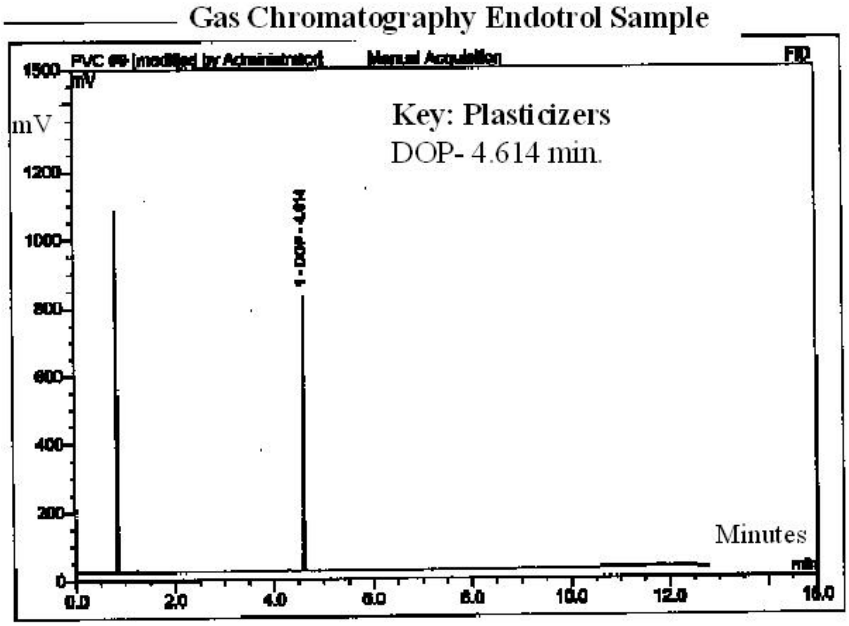


Figure 3.20 Gas Chromatography results for Endotrol endotracheal tube

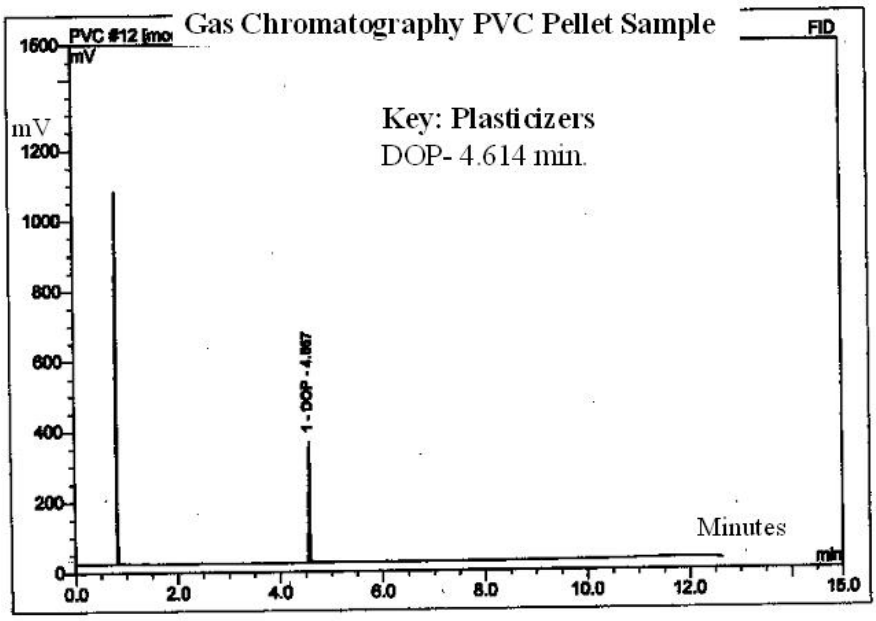


Figure 3.21 Gas Chromatography results for PVC pellets

3.3 Mechanical Analysis Results

3.3.1 Uniaxial Tensile Testing

Tensile testing of dogbone specimens of tube and cuff samples produced the following stress vs. strain graphs. There are slight discrepancies between each trial run, and that is due primarily to the variations between the securing of each sample in the tensile grips before testing. Despite countless attempts, the smallest variation in how the sample was cut and how it lay in the grips could make a huge difference in the results obtained. Some samples fractured in the middle of the dogbone, others near the top, others near the bottom. Stress vs. strain curves for several ET tube and cuff samples are shown below. Additionally, a graph of the curve averages is shown beneath each respective graph.

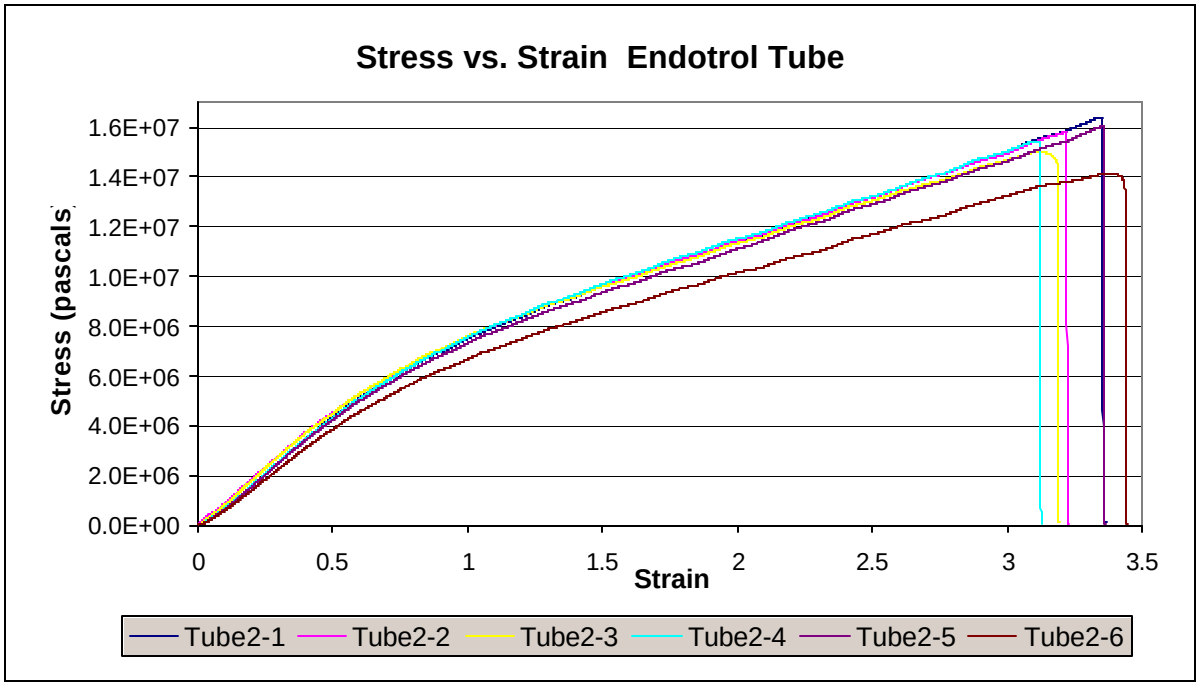


Figure 3.22 Stress vs. Strain curves for six Endotrol tube dogbone specimens

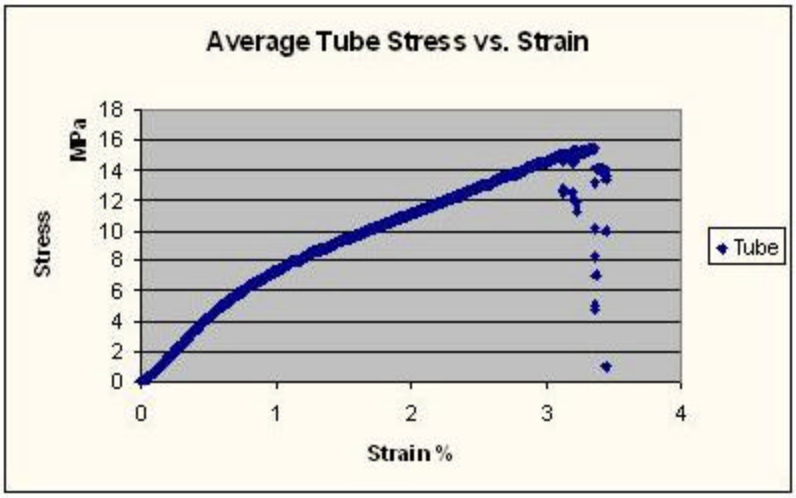


Figure 3.23 Average Stress vs. Strain curves for ET tube samples

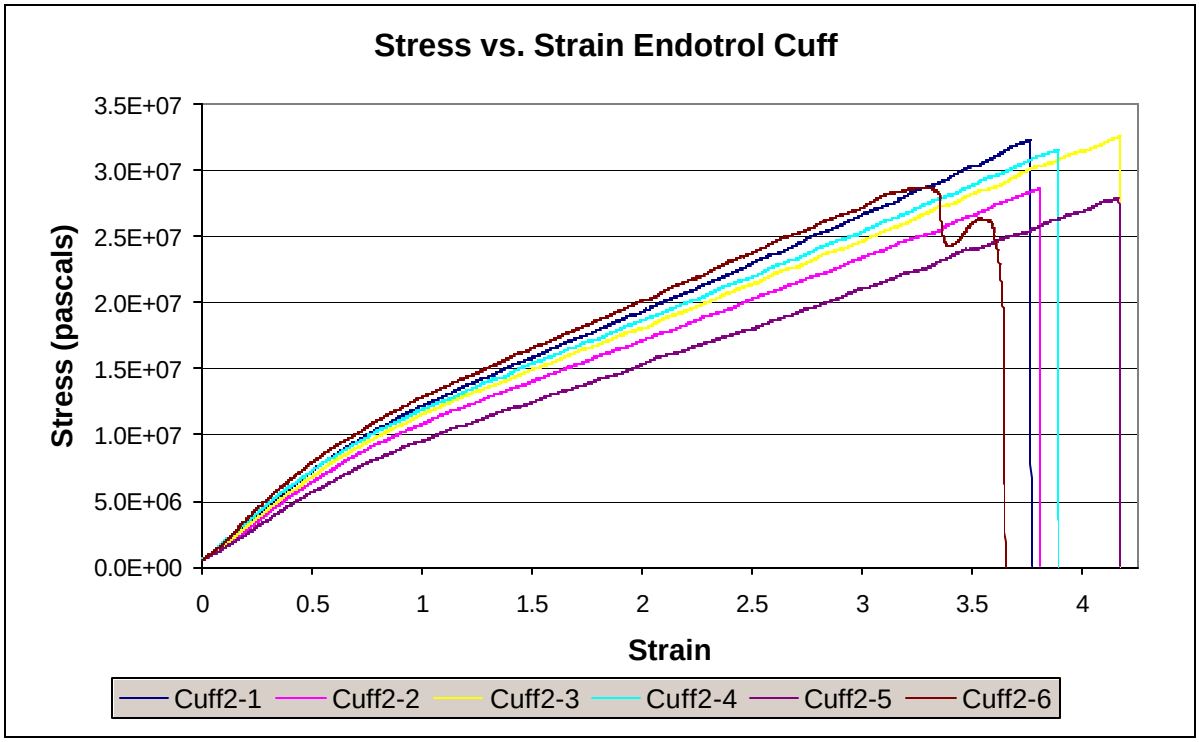


Figure 3.24 Stress vs. Strain curves for six Endotrol cuff dogbone specimens

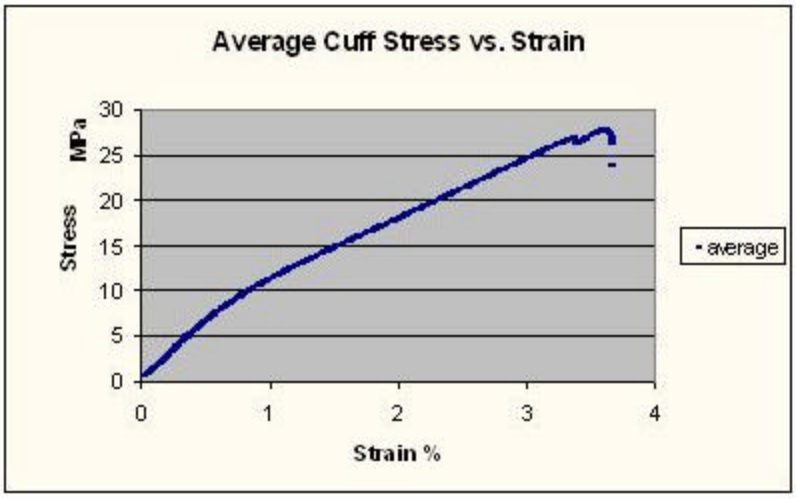


Figure 3.25 Average Stress vs. Strain curves for ET tube samples

Mechanical testing of ET cuff and tube samples gives an average strain that lies between 325-425%. The expected strain for plasticized PVC lies within 250-450%, so these results seem reasonable. The average fracture stress, strain and Young's Modulus for ET

tube was 15.5Mpa, 3.35% and 14.5+/-0.3 MPa, respectively. The average fracture stress, fracture strain and Young's Modulus for ET cuff was 27.1Mpa, 3.635% and 8.45+/-0.15 MPa, respectively. These mechanical tests give insight to the overall properties of PVC/plasticizer used in endotracheal tubes. This information can be used to compare/contrast alternate materials that can be investigated for use in endotracheal tubes.

3.3.2 Injection Molding

Injection molding of PVC pellets at varying durometers allowed the testing of processing techniques, hazards, and machine properties. An average temperature of 275°F was used during processing. A fume hood was necessary, and careful watch was needed. Small dogbone tensile specimen were formed by injection molding of PVC. Preliminary tensile tests revealed a much lower fracture strain than the tested cuff and tube samples, which indicated that several things could be amiss. The processing temperature for PVC may have been too high, altering the molecular properties of PVC. Excess of previously used polymers could have remained in the injection molding machine after flushing with 1-2kg of pellets, thereby affecting the mechanical properties. The processing technique, while toxic, was relatively easy, indicating the ease at which current ETs can be manufactured, despite health and environmental damage issues.

3.3.3 Cuff Herniation Testing

Cuff herniation testing suggested that when the Mallinckrodt Endotrol Tubes were initially inflated they displayed a small, relatively negligible amount of herniation. Measurements were taken around the middle of the cuff at 30 degree increments, which are labeled 1-13. Figure 3.26 shows the circumference of the cuff after being inflated with a medical syringe with the equivalent of 35ml air. Very little herniation is noticeable from the diameter measurements taken.

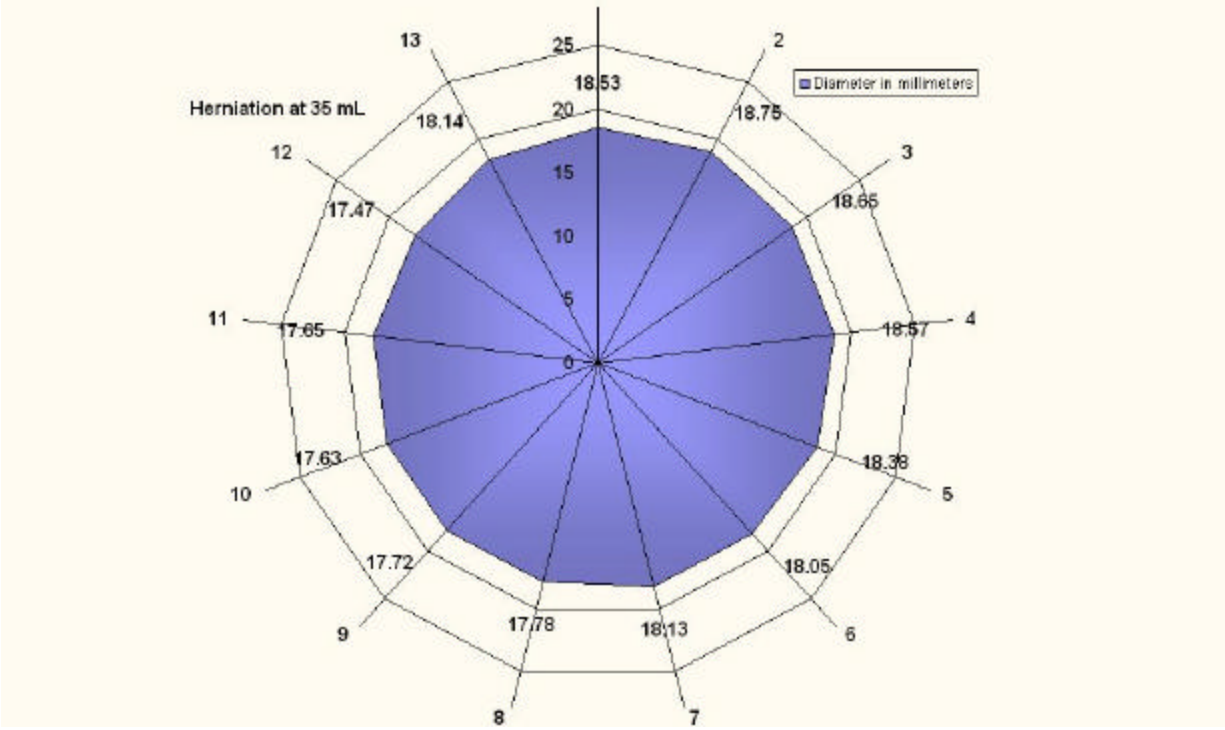


Figure 3.26 Cuff diameter measurements after inflation with 35ml of air

The following two figures present the circumference of the ET cuff upon inflation with 60ml of air and after being left fully inflated with 60ml of air for 24 hours. From these tests, relatively little herniation was noticeable. This suggests that the current endotracheal tube material does, in fact, stand up to the ASTM standards prepared to legalize ET cuffs.

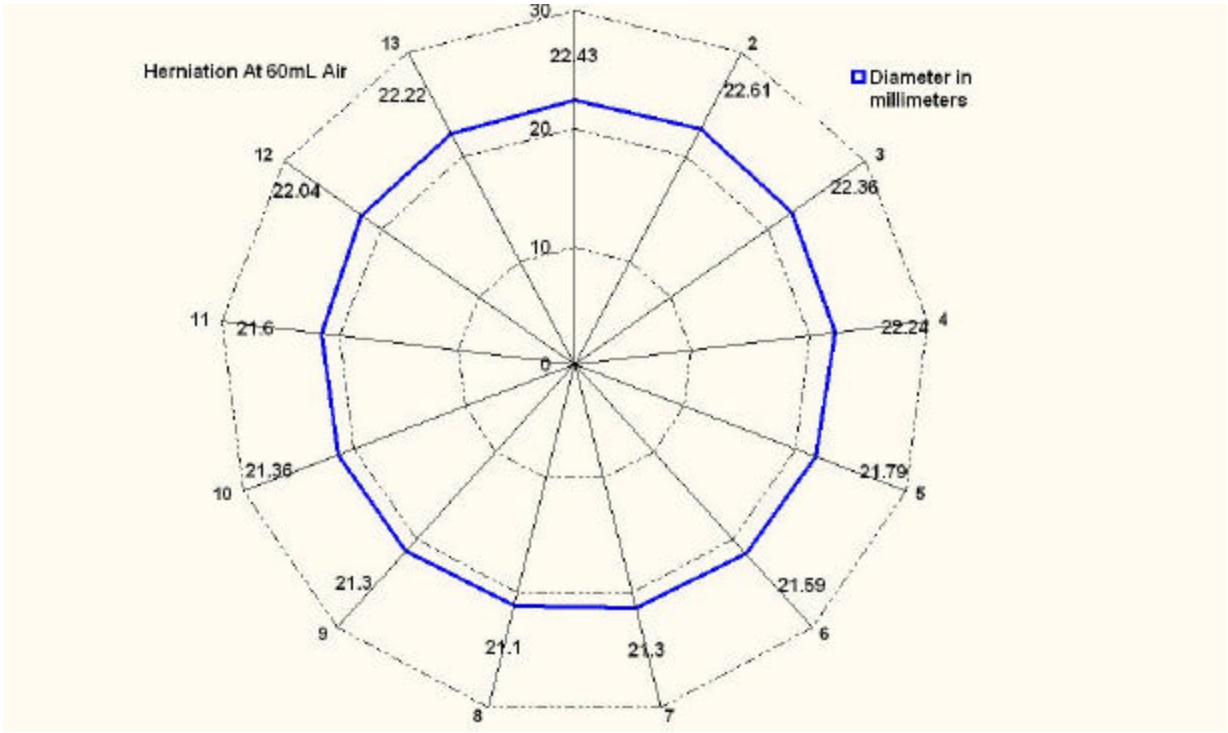


Figure 3.27 Cuff diameter measurements after inflation with 60ml of air

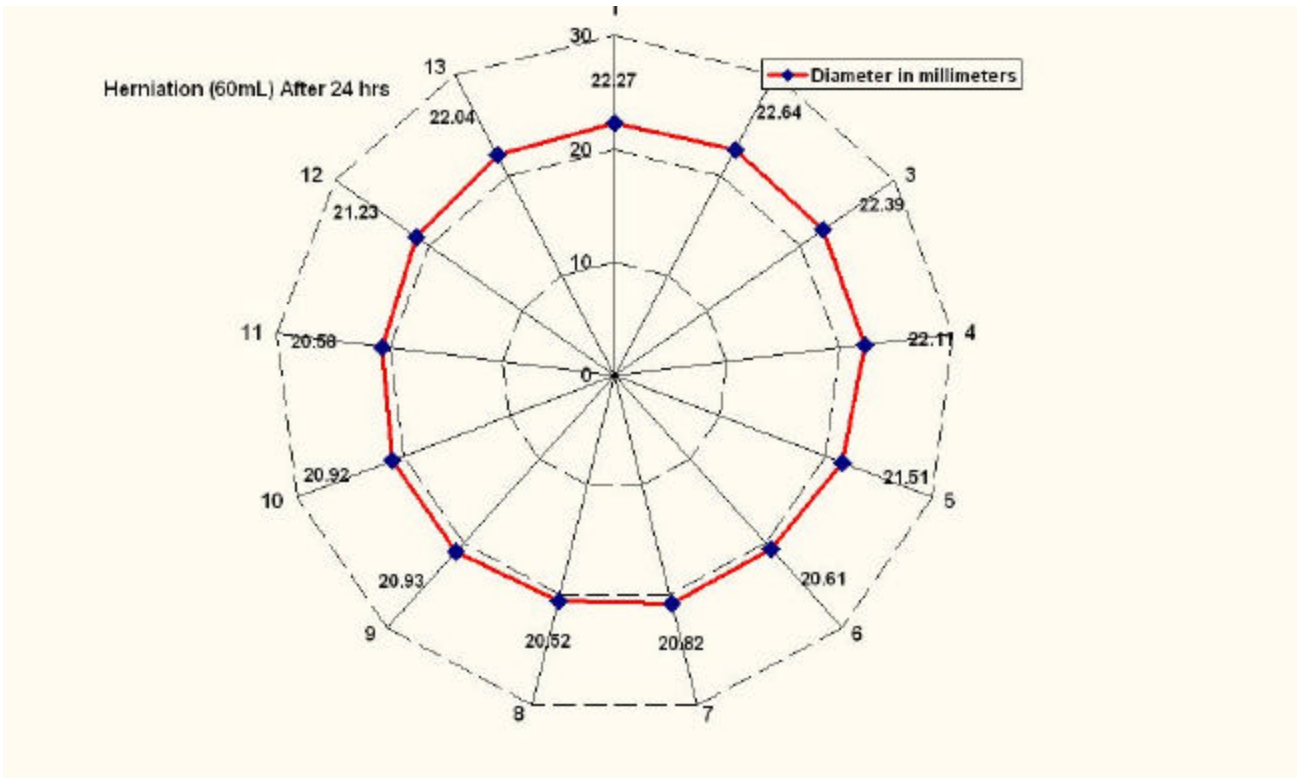


Figure 3.28 Cuff diameter measurements following 24 hr. inflation period

4 CONCLUSIONS

From the investigation of the mechanical, chemical, morphological, and biocompatibility characterization of injection-molded (Endotrol) tubes, it was determined that the tubes were made out of 64.4% poly(vinyl chloride) and 36.6% di-ethylhexyl phthalate (DEHP), also known as di-octyl phthalate (DOP). Detailed processing-structure-property relationships have been investigated. The micro to macro-level experimental procedures used have given property results never before determined about the polymeric material as used in endotracheal tubes.

From the microscopic analysis, surface features, such as plasticizer leaching, polymeric orientation, cuff thickness, and surface adhesive forces were observed. The crystalline surfaces shown in the AFM, SEM and Optical Microscopy images are of surfaces covered in crystals of plasticizer which have leached from the surface. The amorphous polymeric orientation was noticeable through AFM imaging by the random arrangement of the surface features. Cuff thickness was easily determined through SEM imaging to be 40 microns thick, on average. Additionally, surface adhesive forces tested by MFP gave, on average surface forces of 19.6nN in air, and 0.9nN in PBS solution. While these results do not give important information in their present state, these tests can easily be repeated using proteins attached to the cantilever tip, which will give information about the protein-surface interface. This, then, can be used to describe the potential protein-surface interactions between tracheal walls and PVC/plasticizer surfaces. The contact angle measurements show that the surface of ET's are relatively hydrophobic, having an average contact angle measurement equal to 81.5° +/- 6.5°.

Chemical analysis techniques used which included fourier-transform infrared spectroscopy, gel permeation chromatography, differential scanning calorimetry, accelerated solvent extraction, and gas chromatography gave property information about the current ETs. From the analysis techniques, the exact percent plasticizer in ETs was determined to be 36.6%. The type of plasticizer used, DEHP, was also determined through GC tests. From these results, many general ET properties have been determined, which is exciting because these details about ETs are proprietary company information.

Investigative mechanical testing has giving a better understanding of ET properties. The modulus of PVC used, mechanical strength information was all determined through mechanical analysis. With these results, different potential materials can be investigated and more readily analyzed, compared and contrasted to the currently manufactured tubes.

The polymeric materials used in endotracheal tubes have never before been analyzed from micro to macro-scale. The research performed has potential to lead to dramatic results that would forever change the field of biomedical device manufacturing and greatly decrease related patient injury. The results of these studies have formed a basis for future ET materials selection and design.

Though this is the beginning few steps of a much larger project, this thesis research has created a foundation of knowledge that has the potential to help the lives of millions through the improvement of a key medical device currently used in hospitals around the world. With the help and support of doctors, surgeons, and a brilliant MIT Faculty, this project has the potential for great success. Working on this project gives me the great satisfaction of knowing that I am working on a project that has the potential to help suffering patients worldwide.

5 RECOMMENDATIONS

Concerns have risen in regards to the material properties found in endotracheal tubes which have prompted the proposal described in this paper, in which the investigation and improvement of surface properties which will alleviate biofilm, bacterial adhesion and mucous buildup in tubes will be discussed. These concerns regularly cause tube blockage, nosocomial pneumonia and other problems which inhibit proper respiratory care or cause serious illness to occur.

In order to further investigate biocompatibility problems caused by the polymeric material currently in use, nanoscopic analysis and toxicology/biocompatibility studies must be performed to give novel biomolecular results about medical device material. Coating of medical grade PVC/DEHP with hydrophilic materials, such as PEG, will be investigated. Additionally, a microscopic coating with silver alloy material will also be investigated as a means to alleviate bacterial adhesion to the surface. The polymeric materials used in endotracheal tubes have never before been analyzed in such a manner, and the research performed may lead to dramatic results that would forever change the field of biomedical device manufacturing and greatly decrease related patient injury.

Biodegradable polymers, such as PEG, have been under investigation for use in medical devices for the past three decades. These polymers can be either natural or synthetic, but often it appears the synthetic biodegradable polymers are better since they can more readily be formed into a more predictable form during processing. Biodegradable polymers, in general, are chosen so they have mechanical properties to match the desired application, do not invoke inflammatory response, can be metabolized by the body, are easily processed, demonstrate an acceptable shelf life and are sterilized without difficultly.[27]

Recently, synthetic biodegradable polymers are being used or investigated for dental application, wound closures, cardiovascular applications, fixation devices, and drug delivery systems. While the molecular weight of biodegradable polymers is low in comparison with molecular weights used in medical grade PVC, higher molecular weight plastics can be formed. In fact, biodegradable materials are currently being exploited as packaging material. Biodegradable polymers could help alleviate biocompatibility issues in endotracheal tubes by using the hydrophillicity of the polymer as a means of getting rid of biofilm formation. Bacteria, proteins and mucous would be less likely to attach to a highly hydrophilic surface.

Unfortunately, there are a few problems with the application of these concepts. Devices which incorporate biodegradable materials must stay "below the glass-transition temperature in order to keep the polymer from changing during sterilization."[27] Additionally, many of the common biodegradable materials are both expensive, which may cause problems during endotracheal tube manufacturing, and have a relatively quick half life, which could cause serious problems if an endotracheal tube was stored for several months before use. The table below describes the melting point, glass transition temperature, tensile modulus and degradation time for several commonly used biodegradable polymers. The polymers with higher degradation times, PCL and LPLA, also have a relatively low modulus and glass-transition temperature which is not optimal for use in ETs.

Table 5.1 Properties of common biodegradable polymers. [27]

Polymer	**Melting Point (°C)**	**Glass-Transition Temp (°C)**	**Modulus (Gpa)**[a]	Degradation Time (months)[b]
PGA	225—230	35—40	7.0	6 to 12
LPLA	173—178	60—65	2.7	>24
DLPLA	Amorphous	55—60	1.9	12 to 16
PCL	58—63	(—65)—(—60)	0.4	>24
PDO	N/A	(—10)— 0	1.5	6 to 12
PGA-TMC	N/A	N/A	2.4	6 to 12
85/15 DLPLG	Amorphous	50—55	2.0	5 to 6
75/25 DLPLG	Amorphous	50—55	2.0	4 to 5
65/35 DLPLG	Amorphous	45—50	2.0	3 to 4
50/50 DLPLG	Amorphous	45—50	2.0	1 to 2
a Tensile or flexural modulus.				
b Time to complete mass loss. Rate also depends on part geometry.				

After investigation of the biodegradable polymers as a means to improve endotracheal tubes, anti-microbial coatings can be studied as a means to improve endotracheal tubes. The following is a novel idea for how to improve upon the current ETs in an effort to alleviate bacteria and mucous buildup on current tubes.

Recently, research into the effects of antimicrobial agent, silver, in medical devices has been under investigation. These have not yet been implemented in any way with respiratory equipment, in particular endotracheal tubes. Primary focus of companies investigating silver coating have been on devices such as urinary catheters, which are commonly studied because of the likelihood of infection in the patient.[29] It is generally accepted that, in medical devices placed in the body, proteins adsorb to the surface, creating a biofilm which provides anchoring sites for bacteria. This can occur before, during or after implantation. "After successive adhesion, bacterial proliferation gradually leads to the device-related infection."[28] In order to mitigate such infection, surface modification techniques, such as the application of silver ions to a surface have been investigated.

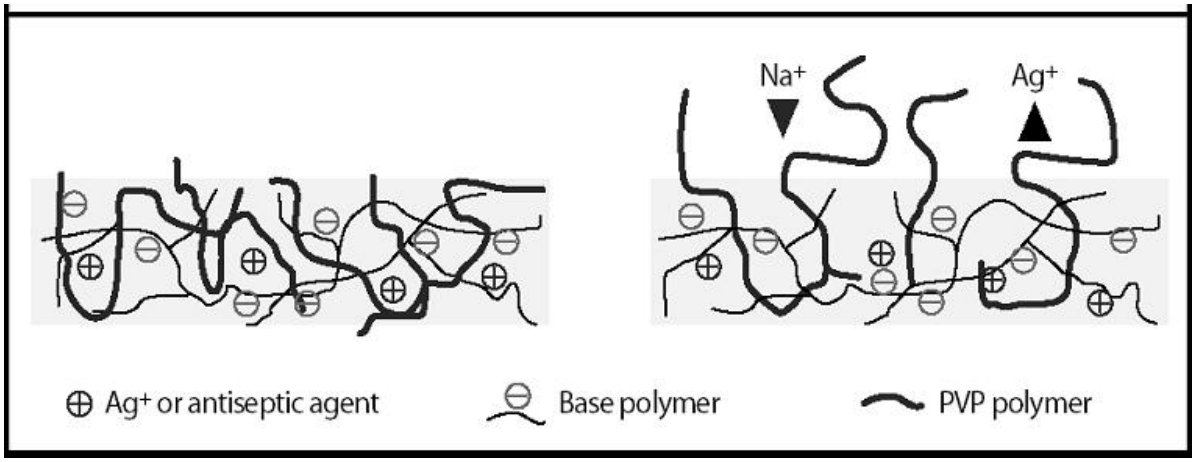


Figure 5.1 Mechanism of controlled, long-term release of silver ions in LubriLAST-K coating [30]

The diagram above demonstrates one method of an antimicrobial coating which uses silver as a means of alleviating bacterial adhesion. In this case, the silver alloys have been implemented as part of the polymeric (polyurethane) coating. This method is built to release ions as a means of being a sort of drug-release method. Degradation problems can occur because debris could potentially trigger inflammation. Shown below is a diagram of

LubriLAST-K, an SEM image demonstrating how the silver ions can alleviate adhesion of bacteria to the surface.

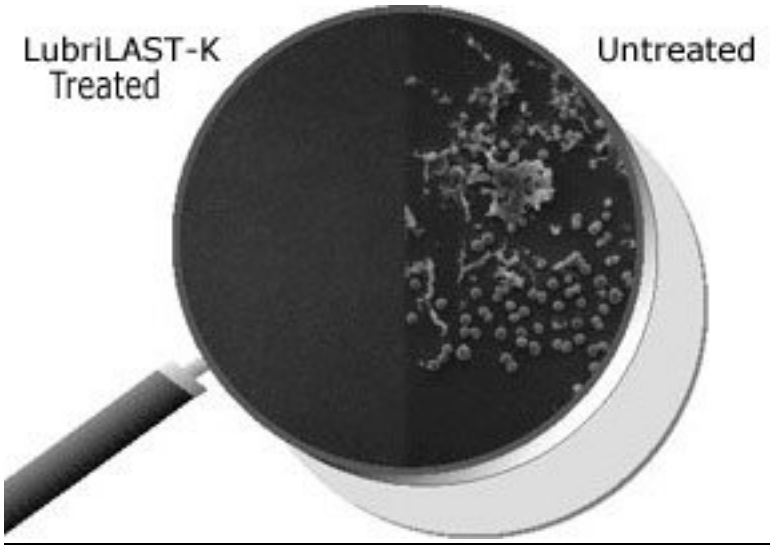


Figure 5.2 SEM Image of bacterial adhesion with and without silver ions present. [31]

Materials can be studied on the nanoscopic scale and results can be compared to those determined for current endotracheal tube material. Micro and nanostructure (e.g. defects, polymeric chain molecular weight and alignment, surface roughness) and biocompatibility (e.g. surface forces measurement, plasticizer leaching) tests will be performed on the polymers under investigation. Once a polymeric compound is deemed optimal for use in an endotracheal tube, a mock tube will be manufactured, and computational methods such as continuum mechanics and finite element simulations of the pressures and stresses in the various parts of the tube will be employed.

6 REFERENCES

1. ASTM Designation: F 1242—96 Standard Specification for Cuffed and Uncuffed Tracheal Tubes
2. Bertora, Mario. Injection Moulding of PVC for Medical Use. Sandretto Industrie S.p.A.
3. Binnig, G., et al. "Atomic Force Microscope." Physical Review Letters. Vol. 56 (9), pp. 930-933, 1986.
4. Center for Devices and Radiological Health, US Food and Drug Administration FDA Article: Safety Assessment of Di(2-ethylhexyl)phthalate (DEHP) Released from PVC Medical Devices. September 5, 2001.
5. Contreras, Arturo. #14 Determination of Plasticizer in PVC by IR or FTIR and a Precipitation Method. Center for Chemical Education, Miami University, Middletown, OH; 1996-1997.
6. Cox, Everard F., M.D. Personal Interview. Nov. 2001. Jan. 2002.
7. Cox, Everard F., M.D. U.S. Patent 4,979,505 *Tracheal Tube.* Dec. 25, 1990.
8. Ellington, J. Jackson. Octanol/Water Partition Coefficients and Water Solubilities of Phthalate Esters. J.Chem.Eng.Data 1999, 44, 1414-1418.
9. Favis, Basil D. and Hua Liang. Surface Modification Strategies for Multi-component Polymer Systems. 2. Study of the Interfacial Tension and Morphology of Linear Low-Density Polyethylene/Poly(vinyl chloride) Blends. Ind. Eng. Chem. Res. 1997, 36, 1211-1217.
10. Griffiths, Saul. *Mini-Jector Instruction Guide.* Personal Interview. 2002.
11. http://64.55.151.178/mdc/microbe.cfm
12. http://scholar.lib.vt.edu/theses/available/etd-10202000-10490059/unrestricted/thesis.pdf
13. http://spectroscopy.lbl.gov/FTIR-Martin/FTIR-Martin_files/frame.htm
14. http://web.mit.edu/cortiz/www/lab.html
15. http://www.arcelorauto.com/v_ang/produits/definitions2.htm
16. http://www.mos.org/sln/SEM/
17. http://www.shu.ac.uk/schools/sci/chem/tutorials/chrom/gaschrm.htm
18. Jaegar, J. Michael MD PhD and Charles G. Durbin Jr. MD. Special Purpose Endotracheal Tubes. Respir. Care 1999;44(6):661-683.
19. Jones, Jeffry H. M.D. *Acute Pneumonia II* UCDMC Volunteer Faculty, Divisions of Pulmonary Critical Care and Infectious Diseases.
20. Kacmerak, Robert, M.D. Personal Interview. April 14, 2003. Dir. Respiratory Care at Mass General Hospital, Massachusetts.
21. Lin, T., Lu, F., Conroy, S., etc. Antimicrobial Coatings:A Remedy for Medical Device-Related Infections. AST Products, Inc. Billerica, Massachusetts, USA. Medical Device Technology, Oct. 2001.
22. Middleton, John C., Tipton, Arthur J. Synthetic Biodegradable Polymers as Medical Devices. Medical Plastics and Biomaterials Magazine. March 1998.
23. MIT Faculty, Staff and Students—DMSE, ME, ChemE
24. Ortiz, Christine, PhD. -- MIT Faculty Advisor

25. Polarized Resonance Raman and FTIR Reflectance Spectroscopic Investigation of the Molecular Orientation in Industrial Poly(vinyl chloride) Specimens. Macromolecules 2000, 33, 5613-5623.
26. Ratner, Buddy D., Hoffman, Allan S., Shoen, Frederick J., Lemons, Jack E. Biomaterials Science: An Introduction to Materials in Medicine. 1996.
27. Shashoua, Yvonne R. Inhibiting the deterioration of plasticized poly (vinyl chloride) – a museum perspective. September 2001.
28. Sigma-Aldrich. Materials Safety Data Sheets located on website: www.sigmaaldrich.com. 2002.
29. Swaille, Beverly. Soxhlet Extraction of Fat from French Fries. University of Cinncinatti, Cincinnatti, OH.
30. Tickner J, Hunt P, Rossi M, Haiarna N, Lappe Ma. 1999. *The Use of Di-2-Ethylhexyl Phthalate in PVC Medical Devices: Exposure, Toxicity, and Alternatives.* Lowell: Lowell Center for Sustainable Production, University of Massachusetts Lowell. Webpage: www.noharm.org.
31. Topulos, George, M.D. Personal Interview. April 15, 2003. Dept. Anesthesiology, Brigham & Women's Hospital, Massachusetts.