COMPARISON OF DIFFERENT CONTRAST AGENTS WHEN IMAGING SHAPE MEMORY POLYMER FOAMS

A Senior Scholars Thesis

by

SCOTT EVERETT EAGLESTON

Submitted to Honors and Undergraduate Research
Texas A&M University
in partial fulfillment of the requirements for the designation as

UNDERGRADUATE RESEARCH SCHOLAR

May 2012

Major: Biomedical Engineering

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Approved by:

Research Advisor: Duncan Maitland
Associate Director, Honors and Undergraduate Research: Duncan Mackenzie

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ABSTRACT

Comparison of Different Contrast Agents When Imaging Shape Memory Polymer Foams. (May 2012)

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SMP foams have unique properties that make them well suited for certain medical applications. SMP foam has the ability to be programmed to "remember" a temporary shape, and once heated can revert back to its original shape. Scientists have recognized that shape memory foam might have great value in the medical industry. One application for SMP foam that is being developed is an embolic device for the treatment of cerebral aneurysms. One critical component in the development of these foams is the creation of accurate 3D models of the foam to determine strut thickness, pore cell size, anisotropy, and perform flow simulations. To obtain a 3D model of these low density polyurethane foams, they must be imaged using μ-CT. In some cases a contrast agent must be used in order to see the foam when imaging via μ-CT, so an appropriate contrast agent must be determined. Different contrast agents at various concentrations were tested in order to find one that is suitable for this application. Barium sulfate, tungsten, and tungsten carbide were all tested at 1%, 5%, 10%, 25%, and 50% by mass concentrations. The 5% barium sulfate samples produced the best results, although they

were still not good enough to produce an accurate 3D model, so further research will need to be conducted.

DEDICATION

This is dedicated to my beautiful fiancée Stefanie, and to anyone whose life has been touched by the devastating effects of cerebral aneurysms.

ACKNOWLEDGMENTS

I would like to thank my advisor Dr. Duncan Maitland for encouraging me to do this project in the first place, and for giving me the necessary resources to complete it. I would also like to thank Jennifer Rodriguez for helping me develop the idea behind this project and the procedure for completing it. She was also the main person I could go to anytime I needed help. Finally, I would like to show my gratitude to Trevor Lancon who tirelessly imaged all of the foam samples for me. Without these people, and the support of friends and family, this project would not have been a success.

NOMENCLATURE

SMP	Shape Memory Polymer
3D	Three Dimensional
CFD	Computational Fluid Dynamics
μ-CT	Micro-Computed Tomography

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CHAPTER I

INTRODUCTION

Foams have many uses in our society due to their unique properties. In everyday life we encounter foams in the form of soap froths, shape memory mattresses, and bread, but the use of foams can be extended into biomedical applications such as the medical device industry. The unique properties of foam include low density, ability to insulate, and the ability to cushion. Foams have a complex structure that make it difficult to define their 3D geometry, especially when pore cell sizes are less 1000 μm, but these characteristics must be determined to further our understanding of SMP foam and to eventually run computer simulations, such as CFD, based on the foam.

Foam structure

Foams are 3D networks of gas filled cells [1]. There are four main structures that define the 3D geometry of foam: struts, vertices, windows, and cells[1]. The struts provide the structural stability in the foam and can be compared to struts in a bridge or a building. Vertices are created when two or more struts meet at a point, windows are created when struts form a closed loop, and cells are created when windows connect to form a closed volume [2]. Figure 1 shows a representative cell of foam. Foam can be either closed

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This thesis follows the style of *IEEE Reviews in Biomedical Engineering*.

cell or open cell [2]. Closed cell foams have thin membranes that close off the windows, and open cell foams have open windows [2]. Closed cell foams and open cell foams have different properties and therefore are used in different applications. Closed cell foams act as good insulators because the air trapped inside the cells slows down heat transfer [3]. Open cell foams can act as filters because the open structure allows fluids to pass through, or they can act like cushions because they have the ability to dissipate a great deal of energy [3].

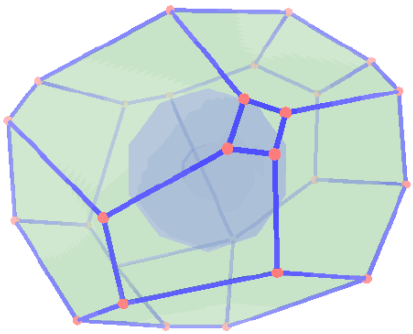

Fig. 1. One cell of SMP foam. All of the structures of foam can be seen clearly here. The orange circles are vertices, the blue lines are struts, the light green spaces between the blue lines are windows, and the blue sphere in the middle represents the middle of the cell.

Shape memory capabilities

The foam characterized in this research is a polyurethane based SMP foam. SMP foam has the ability to actuate back to a remembered primary configuration after being formed into a secondary configuration [4]. This process is illustrated in more depth in Figure 2.

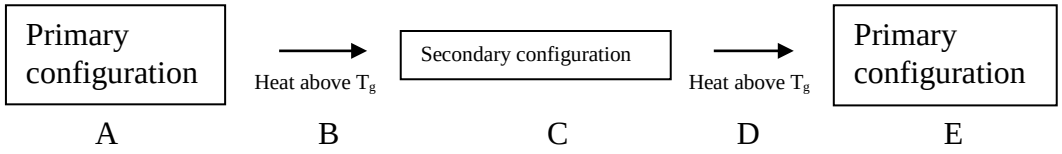

Fig. 2. Shape memory properties of SMP foam. A) Foam is formed and machined into its primary configuration. B) Foam is heated above its transition temperature, in this material its glass transition temperature (T_g). C) The foam is then formed via force into a secondary configuration and cooled so it will maintain the secondary configuration. D) Foam is heated above the T_g again. E) Foam actuates back to the primary configuration.

SMP foam has many potential uses in the medical field because of its unique properties. The SMP foam evaluated in this research is being developed to treat cerebral aneurysms [5], [6], [7]. The goal of this treatment is to insert the foam into the aneurysm by way of a catheter and then actuate it so the foam fills the aneurysm sac. The foam will then induce a clotting response which will ultimately eliminate the threat of potential aneurysm rupture[2].

Aneurysms

Cerebral aneurysms are structural abnormalities of an artery wall located in the brain. The abnormalities reduce the structural stability of the artery and increase the risk of rupture. The risk associated with aneurysms is that the artery will rupture, resulting in internal bleeding that can kill or cause severe mental handicap in the patient [1], [8].

A commonly used treatment for cerebral aneurysms is the use of endovascular coiling [9]. Endovascular coiling involves releasing platinum coils into the aneurysm that will induce a clotting response from the patient. The SMP foam works in much the same

way, but it should provide a better tissue scaffold than the platinum coils, which should result in a better *in vivo* healing response [2]. The foam should avoid some of the problems associated with endovascular coiling as well. The platinum coils that are currently used are at risk of dislodging from the aneurysm sac or of rupturing the weak wall of the aneurysm with its sharp edges, both of which can cause disaster for the patient. The SMP foam is designed to have greater stability in the aneurysm and should not rupture the aneurysm as easily as the coils, making the foam a safer alternative [10].

Imaging

Imaging the foam so the structure can be analyzed is a crucial step in studying and developing the foam. Ultimately, the imaging process should provide models that can be used to run CFD simulations so that the foam's mechanical interaction with blood can be determined. μ-CT is a useful tool when imaging foams. A 3D image data set obtained from μ-CT is a reconstruction that is created from many individual X-ray images taken over 360 degrees of the volume of the sample. The individual images are created when the X-rays that pass through the specimen and are attenuated. The differences in the attenuation of the X-rays are detected, and then the individual X-ray images produce the 3D image dataset through the process of back-projection summation reconstruction. When a specimen is imaged using μ-CT a resultant stack of images is created that represent the 3D volume of the specimen. The low density SMP foam is not radio-opaque when imaged using a high powered μ-CT machine like the X-Tek Hawk 160XI, which is readily available to the Biomedical Engineering department at Texas A&M

University, so contrast agents must be used to attenuate the X-rays, which causes the negative space in the foam to be imaged.

Contrast agents

For this application and imaging modality, a contrast agent is something that can be used to attenuate X-rays. Contrast agents are commonly used in the medical field when doctors need to take an X-ray of a patient's vasculature or intestines. Barium sulfate is commonly used when imaging the digestive tract and is usually administered orally or through an enema. Iodine is usually used when imaging the vasculature or the urinary tract, and it is usually administered through a hypodermic needle. There are several factors that influence the effectiveness of contrast agents which include the Z number of the elements, the concentration, and the amount used. High Z-element materials attenuate more X-rays than low Z-element materials.

Experimental system

The objective of this research is to determine a contrast agent that provides accurate μ-CT scans that can be used to create 3D models of these foams. Currently, barium sulfate is being used as the contrast agent, but it is unknown whether it resolves the boundary between cells optimally. Different contrast agents will be tested at various concentrations to determine which one is optimal for this application. The data obtained from using the contrast agents will be analyzed using computer programs to determine which agent resolved the boundaries between cells the best. Optimizing the contrast

agent and determining the proper concentration should allow detailed images of the foam to be obtained, which are necessary to construct the 3D model. The model of foam will be used to run flow simulations that can be used to predict the foam's hemodynamic interactions *in vivo*.

CHAPTER II

METHODS

The SMP foam used in this experiment is not radio-opaque when imaged using a high powered μ-CT machine. The polymer does not attenuate the X-rays enough for the researcher to be able to differentiate between the foam and pores in the image data. In order to remedy this problem a contrast agent must be used. There were three different contrast agents tested in this experiment: barium sulfate, tungsten, and tungsten carbide. Different concentrations of each were tested so that the optimal concentration of each could be determined. The next sections will detail how the individual samples of contrast agent embedded foam were created and analyzed.

Preparing the foam

The first step is to prepare the SMP foam for use. The foam comes in roughly cylindrically shaped blocks that are too large to use, so the first step is to cut a one centimeter cross section out of the foam using either a razor blade or a band saw. Next, a biopsy punch is used to punch out the desired number of samples of foam. The edges of the initial block of foam are usually unusable due to boundary constrictions of the foaming container upon fabrication, so the samples should be taken out of the center of the block of foam. In this experiment a 5 mm biopsy punch was used. A 5 mm biopsy punch was used in order to get a small enough sample to be imaged at high resolution with the μ-CT scanner field of view. Next, the foam is heated on a hot plate to 100°C.

Once the foam is heated it is taken off of the hot plate and flattened axially. Because of the unique properties of the SMP foam, the foam holds the flattened secondary configuration once cooled. This was performed to reduce the number of bubbles in the final sample and to induce uptake of contrast agent throughout the volume of the foam. The samples are then set aside until they are needed again.

Preparing the contrast agent

First, the desired contrast agent and concentration of contrast agent must be determined. The concentration of the contrast agent can be measured in two ways: mass percent and volume percent. Mass percent was used for this experiment because of the ease of preparation. For this experiment 1%, 5%, 10%, 30% and 50% by mass concentrations of each contrast agent were used.

The contrast agent must be suspended in agar so that the foam can be embedded in the contrast agent. To prepare the agar and the contrast agent, the proper ingredients must be measured. Table 1 below shows the amounts of the agar, deionized water, and contrast agent that need to be measured for different concentrations of contrast agent.

TABLE 1
RECIPE FOR CONTRAST AGENT MIXTURE AT DIFFERENT CONCENTRATIONS

	Agar (g)	DI water (ml)	Contrast agent (g)
5% by mass	0.69	30	1.62
10% by mass	0.69	30	3.41
25% by mass	0.69	30	10.23
50% by mass	0.69	30	30.69

The agar and the deionized water are mixed together in a beaker and put on a hot plate at 140°C. The mixture must be stirred occasionally and left on the hot plate until the solution begins to boil and bubbles start to form on the bottom of the beaker. While the agar is heating up, the contrast agent can be put in a Flacktek mixing cup. Once the agar is heated up, it is poured into the mixing cup over the contrast agent. The cap of the cup is quickly screwed on and the cup is placed in the mixer at 3700 rpm for 30 seconds. This needs to be performed quickly so that contrast agent mixture is still hot for the next step.

Embedding the foam in contrast agent

The hot mixture from the previous section is then poured over the prepared, compressed samples of foam. The hot contrast agent causes the samples of foam to increase its temperature above the glass transition temperature and actuate back to its primary configuration, which is a cylindrical foam sample 1 cm in height and 0.5 cm in diameter. The actuating process causes the contrast agent to be drawn into the pores of the foam. As the samples cool the contrast agent mixture will solidify. The samples of foam then

need to be cut out of the agar, sealed in an air tight container and stored in a refrigerator. The foam can now be imaged via µ-CT.

Imaging and comparing the samples

Once the foam samples are embedded in contrast agent, they can be imaged using µ-CT. The µ-CT process results in stacks of images that can be used to recreate a 3D model of the foam. Because the µ-CT machine being used cannot "see" the foam, the actual data that comes from this process is the negative space that is in the foam. Once all of the foams had been imaged, the efficacy of the different contrast agents has to be determined. This process can be performed through visual inspection. Once the best contrast agent and concentration has been determined, the best image set can be used for analysis with different 3D analysis software.

Analyzing the foam

The stacks of images that are the product of µ-CT can be imported into 3D image segmentation software. Amira 5.4 (Visage Imaging, Richmond, VIC, Australia) was used in this experiment. The first step in creating a 3D model from stacks of images is to segment the images. Segmenting allows the user to define regions of interest, such as defining what is foam and what is not foam in the images. Segmenting can be done in many different ways, some simple and some complex. The simplest way to segment an image is to define pixel values that correspond to different structures, this is known as thresholding. Thresholding can only be performed effectively with very high quality

data sets. If the data set is noisy or blurry filters must first be used to clean up the data before the foam can be segmented. Once the data has been cleaned up, more sophisticated segmentation algorithms can be used, such as level set or watershed segmentation. Once the images are properly segmented, a 3D surface of the foam can be created. The hope is that the 3D models will be accurate enough to eventually run CFD simulations.

Another program that can be used during foam analysis is FoamView (University of Minnesota). FoamView is a program that was developed specifically to analyze foams, and it can give different statistics about the foam, such as strut length distribution and pore volume distribution. Binary image data that represents the volume can be imported into FoamView. The image data from Amira can be converted into binary data using MATLAB (MathWorks, Natick, Massachusetts). FoamView can then take that data and run a thinning algorithm on the foam struts to create a 'skeleton' of the foam data. The skeleton is then used to create a 'stick figure' of the foam. FoamView then uses this stick figure to calculate different statistics about the foam.

CHAPTER III

RESULTS

Over the course of this experiment, samples of SMP foam were embedded in different contrast agents at various concentrations and then imaged using μ-CT. Barium sulfate, tungsten, and tungsten carbide were the contrast agents used, and they were each tested at concentrations of 50%, 25%, 10%, 5%, and 1% by mass. The following sections detail the results of this experiment.

Measurement data for the embedded foam samples

All of the ingredients that were used to make the embedded foam samples were measured out by hand, and therefore, were subject to human error. Table 2 below shows the measurements that were made when making the samples, and the actual concentrations of each of the samples. The actual concentrations of the contrast agents were calculated using the following formula.

$$concentration = \frac{mass\ of\ contrast\ agent}{mass\ of\ contrast\ agent * mass\ of\ water * mass\ of\ agar}$$

20 mL of deionized water were used to make each of the samples. Due to the density of water being 1 g/ml, 20 g was assumed to be the mass of the water in the calculations.

TABLE 2
ACTUAL MEASUREMENTS OF INGREDIENTS USED WHEN MAKING SAMPLES

Contrast Agent	Ideal Concentration (% by mass)	Mass of agar (g)	Mass of contrast agent (g)	Actual Concentration (% by mass)
Barium Sulfate	50%	0.460	20.50	50.05%
Barium Sulfate	25%	0.470	6.832	25.02%
Barium Sulfate	10%	0.466	2.261	9.95%
Barium Sulfate	5%	0.476	1.083	5.02%
Barium Sulfate	1%	0.471	0.312	1.50%
Tungsten	50%	0.463	20.40	49.92%
Tungsten	25%	0.462	6.836	25.04%
Tungsten	10%	0.463	2.286	10.05%
Tungsten	5%	0.465	1.08	5.01%
Tungsten	1%	0.462	0.313	1.50%
Tungsten Carbide	50%	0.475	20.49	50.02%
Tungsten Carbide	25%	0.470	6.824	25.00%
Tungsten Carbide	10%	0.463	2.30	10.10%
Tungsten Carbide	5%	0.466	1.07	4.96%
Tungsten Carbide	1%	0.463	0.315	1.52%

CT data

After all of the samples were made, they were sent off to be imaged using μ-CT. The resultant data from the μ-CT process is a stack of images that represents the 3D object. Each image stack was reconstructed using 360 different X-ray projections taken at different angles. Each of the following figures (Fig. 3-Fig. 10) is a single image taken from one of the image stacks.

The 50% by mass samples were never imaged because the agar never solidified properly. Also, it was observed that none of the contrast agents penetrated the foam at the 25% and 10% by mass concentrations. To validate that observation the 10% and 25% tungsten carbide samples were imaged, and when the results confirmed the observations

it was decided that the 10% and 25% barium sulfate and tungsten samples would not be imaged.

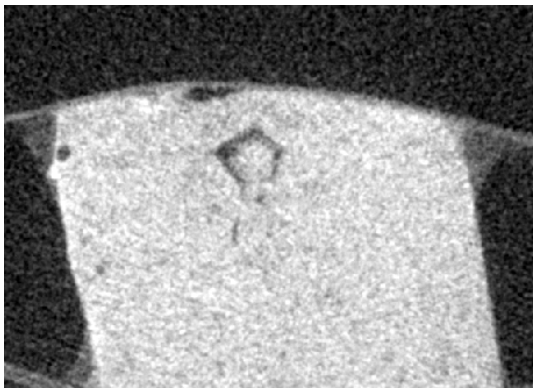

Fig. 3. 1% barium sulfate sample.

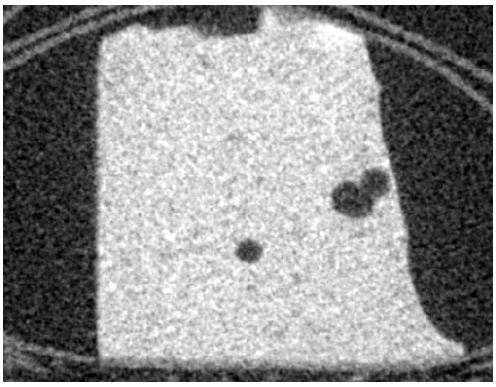

Fig. 4. 1% tungsten carbide sample.

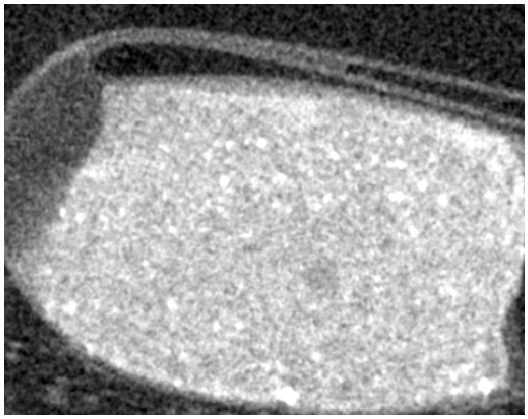

Fig. 5. 1% tungsten sample.

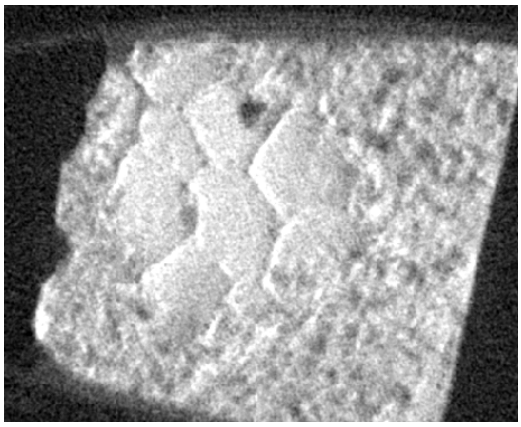

Fig. 6. 5% barium sulfate sample.

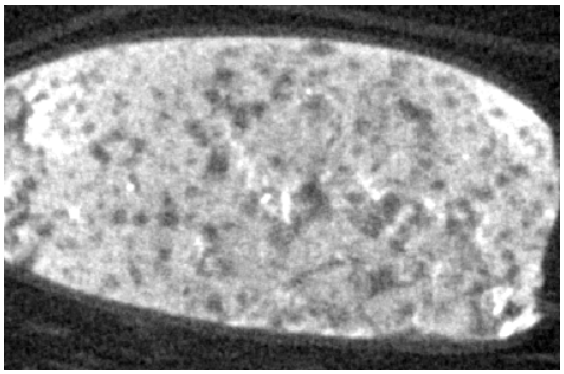

Fig. 7. 5% tungsten carbide sample.

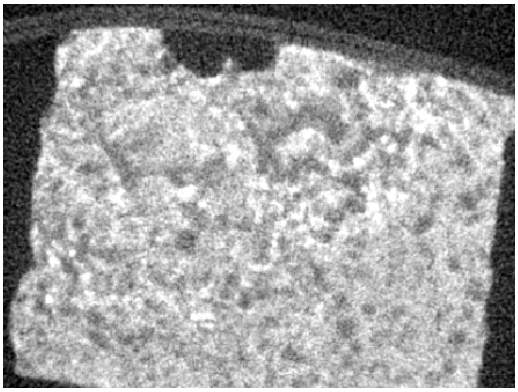

Fig. 8. 5% tungsten sample.

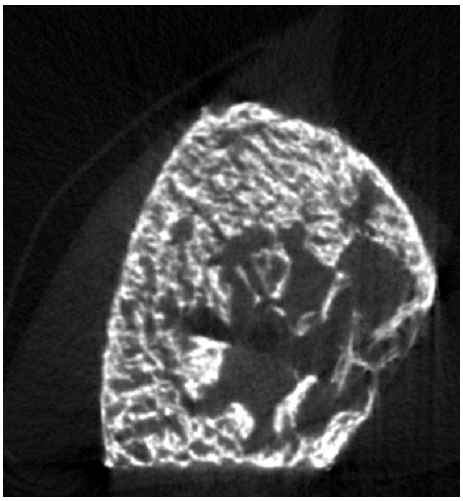

Fig. 9. 10% tungsten carbide sample.

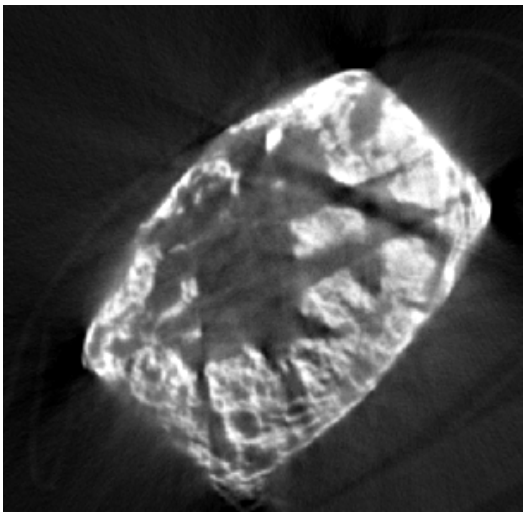

Fig. 10. 25% tungsten carbide sample.

The 50% by mass samples were never imaged because the agar never solidified properly. Also, it was observed that none of the contrast agents penetrated the foam at the 25% and 10% by mass concentrations. To validate that observation the 10% and 25% tungsten carbide samples were imaged, and when the results confirmed the observations it was decided that the 10% and 25% barium sulfate and tungsten samples would not be imaged.

After imaging the foams it was obvious through visual inspection that the 5% barium sulfate sample produced the highest quality data sat, so that sample was imaged a second time using 1000 projections to produce a higher resolution data set. Figure 11, below on the left, shows the 5% barium sulfate sample imaged with 1000 projections, and Figure 12, below on the right, shows it imaged with 360 projections.

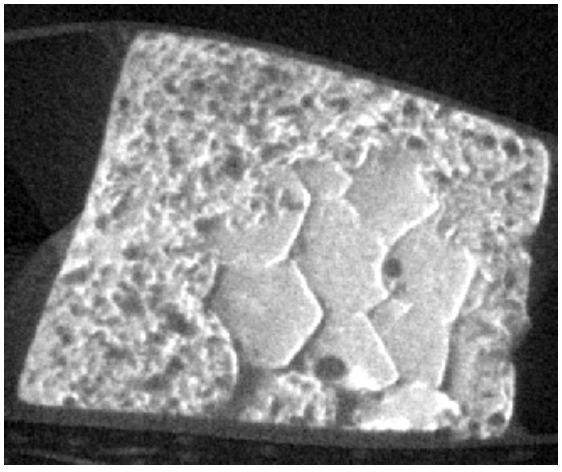

Fig. 11. 5% barium sulfate imaged with 1000 projections.

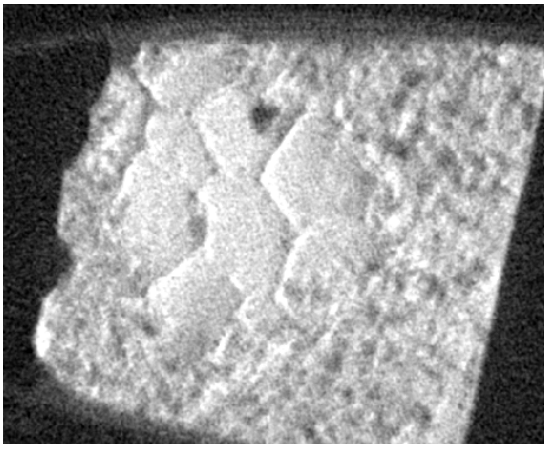

Fig. 12. 5% barium sulfate imaged with 360 projections.

This sample was the only sample where all of the major structures of the foam could clearly be identified.

Foam statistical data

Next, the 1000 projection 5% barium sulfate sample was analyzed using Amira and FoamView. Amira is a computer program that is primarily used to construct 3D models, and FoamView is a program that was developed specifically to extract statistical information from foams.

Amira

To create accurate 3D models using Amira, the quality of the raw data must be very high. Even though the 5% barium sulfate data was much better than all of the other data sets, it was still not good enough to create an accurate 3D model of the foam, but there was still some useful information that could be extracted from the data. Even though the data was not of high enough quality to create a 3D model, the data was still good enough that the major features of the foam can be seen with the naked eye. In foam, struts are located anywhere where three cells meet. Using that principle as a guide, the struts of the foam were manually traced through the foam using Amira. Figure 13 below shows five struts highlighted.

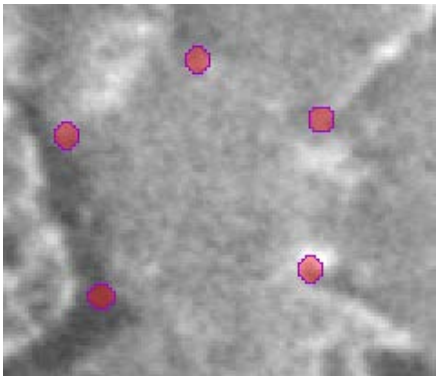

Fig. 13. One cell of foam with the struts highlighted.

Once all of the struts were selected, the data was saved as binary black and white data. Figure 14 below is an example of what the data looked like after it was saved. The struts of the foam are white, and everything else is black.

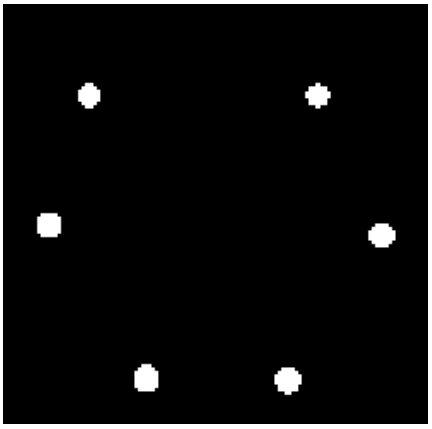

Fig. 14. Struts saved as binary data.

FoamView

MATLAB was then used to convert the data into a ".bin" file type, which can be read into FoamView as a volume. Figure 15 below shows the volume that was read into FoamView.

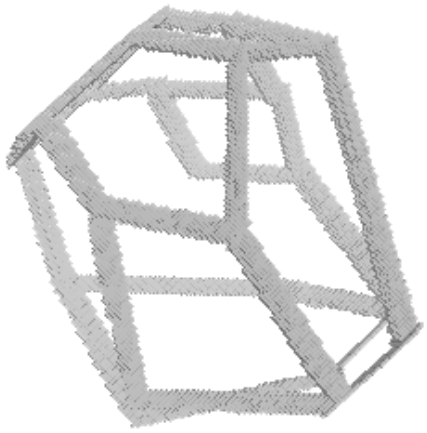

Fig. 15. One cell of foam represented in FoamView as a volume.

A thinning algorithm was then applied to the struts to create a stick figure that represented the foam, as shown in Figure 16. Statistical data was then extracted from the foam. Figures 17-21 show all of the data that was generated by FoamView.

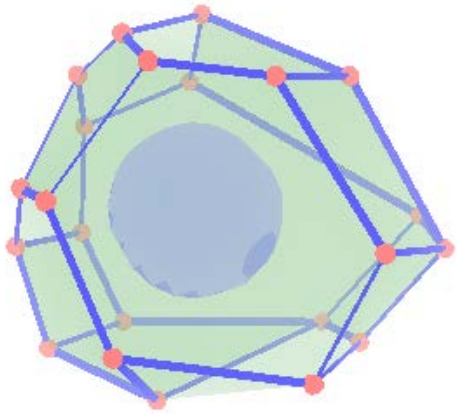

Fig. 16. One cell of foam represented in FoamView as a stick figure.

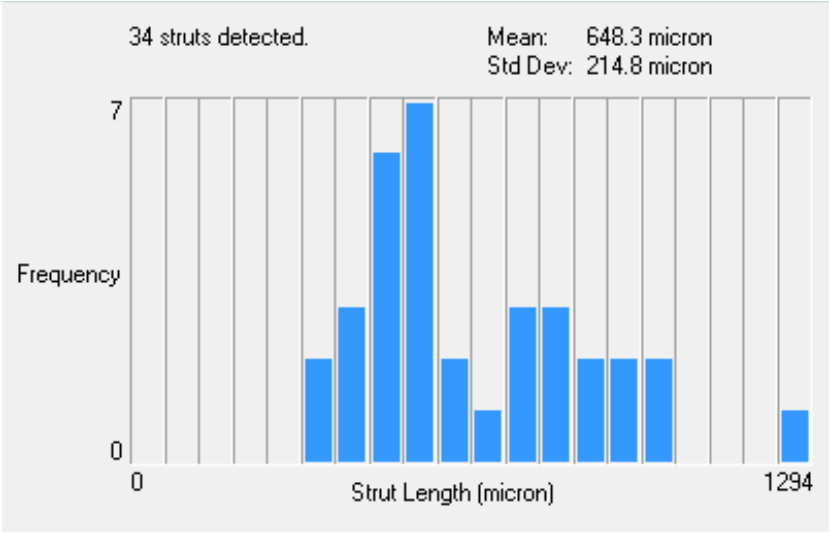

Fig. 17. Strut length distribution. The histogram shows the distribution of strut lengths in the foam.

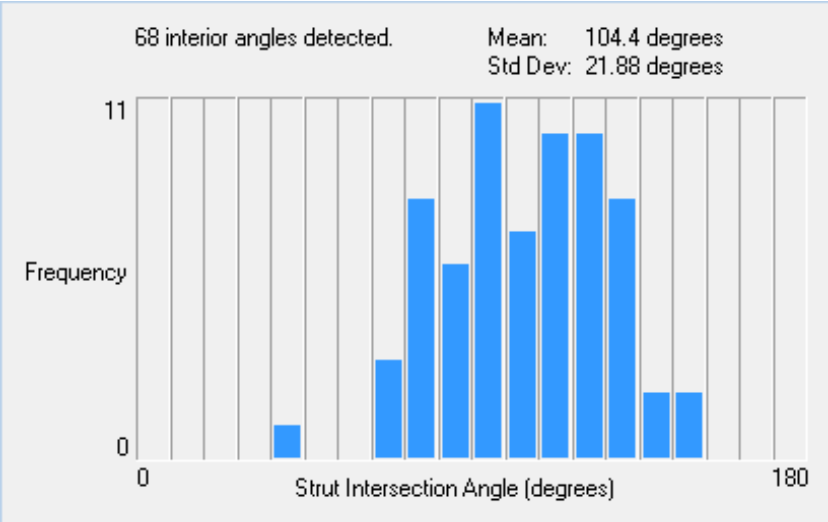

Fig. 18. Distribution of the internal angles of strut intersection within the foam.

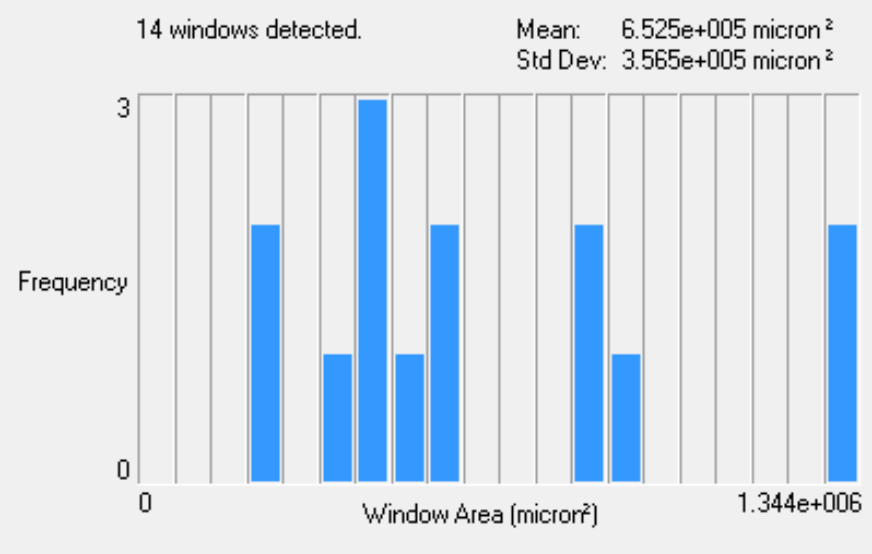

Fig. 19. Distribution of window area within the foam.

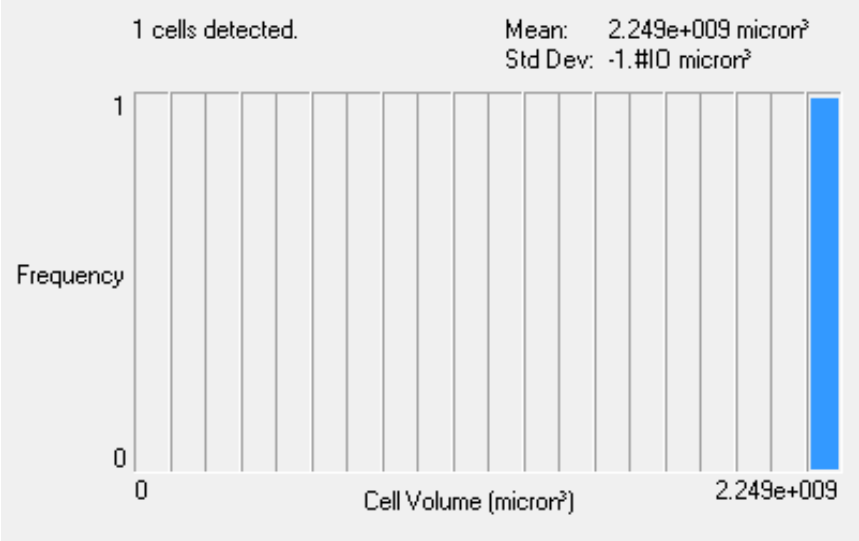

Fig. 20. Distribution of cell volume within the foam. There was only one cell of foam that was analyzed, so that is why only one appears on the distribution above.

Dataset Information

Original Volume File	volume.vtk
Analysis Date	Mar 02, 2012
Voxel Resolution	282x272x388
Voxel Size	16x16x16
Sample Volume	1.219e+011
Surface Detail Level	

Struts

# detected:	34
Lengths:	
Mean	648.26
Std. dev	214.76
Min	375.23
Max	1294.1

Mean orientation vector:
x: 0.559
y: 0.543
z: 0.626
Anisotropy ratio: 1.15

Basic Measurements

Surface Area	
Solid Volume	1.5171e+008
Solid Fraction	0.0012
SA:Volume Ratio	

Windows

# detected:	14
Areas:	
Mean	6.5252e+005
Std. dev	3.5654e+005
Min	2.4671e+005
Max	1.344e+006

Window shape distribution:

0 Triangles	3 Hexagons
5 Quadrilaterals	0 Heptagons
6 Pentagons	0 8+-gons

Connectivity

# vertices:	22
Interior Angles:	
# detected	68
Mean	104.36 degrees
Std. dev	21.88
Min	37.23
Max	150.08

Cells

detected: 1

	Mean	Std. dev	Min	Max
# sides	14	-1.#IO	14	14
Avg. window shape	4.857	-1.#IO	4.857	4.857
Volume	2.249e+009	-1.#IO	2.249e+009	2.249e+009
Surface area	9.135e+006	-1.#IO	9.135e+006	9.135e+006
Isometric quotient	0.751	-1.#IND0	0.751	0.751

All length measurements in micron. Area measurements in micron². Volume measurements in micron³. Angle measurements in degrees.

Fig. 21. Table of statistics. This table shows all of the statistical information about the foam that FoamView can generate.

CHAPTER IV

CONCLUSIONS

Out of all of the the embedded SMP foam samples that were tested, the 5% barium sulfate sample produced the best results. None of the other samples produced data that would be useful for producing 3D models of the foam, but there are still conclusions that can be drawn from the data.

Interpretation of μ-CT results

The results show that no useful data was obtained from the samples when the concentration of the contrast agent was either too high or too low. The 1% by mass concentration samples produced no usable data, which indicates that the concentration of contrast agent was not high enough to adequately attenuate the X-rays of the μ-CT machine. Figure 22 below shows the 1% by mass concentration results. Notice that the structure of the foam cannot be seen in any of the pictures.

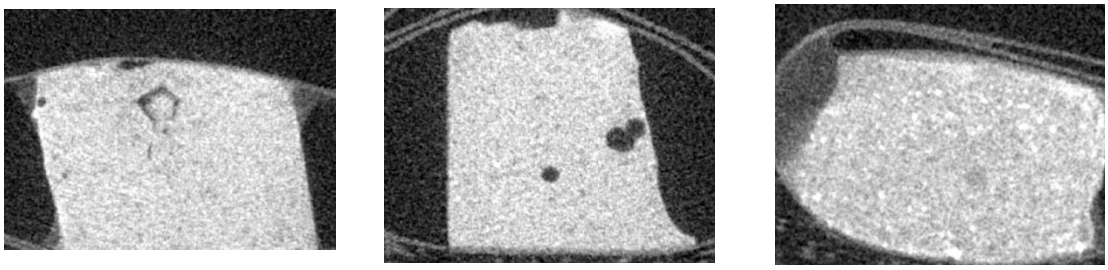

Fig. 22. 1% by mass concentration results. The foam cannot be seen in the 1% by mass concentration results.

The 10% and 25% by mass concentration samples were also unable to produce any usable results, but for a different reason. It can be seen in Figure 22 that the contrast agents at the higher concentrations did not penetrate the foam. The dark spots in the images are the foam samples. The fact that the contrast agents did not penetrate the foam at the higher concentrations indicates that the contrast agent mixture was too viscous to permeate the pores of the foam as it actuated back to its primary configuration.

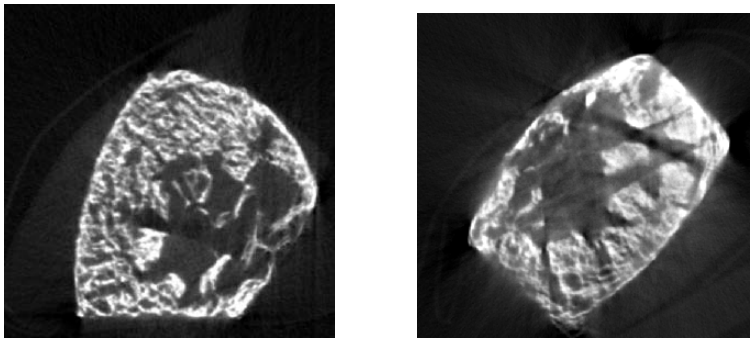

Fig. 23. High concentration results. The contrast agent did not penetrate the foams at the higher concentrations

The previous conclusions, along with the fact that the 5% barium sulfate sample produced promising results, leads to the conclusion that there may be a middle ground concentration that can be found for certain contrast agents that produces quality data that can be used to create a 3D model of the foam.

Interpretation of Amira and FoamView results

In this experiment, a 3D model of the foam could not be created using Amira because the μ-CT data did not contain a sufficient amount of detail, but Amira was still used to manually define the struts of the foam so that FoamView could be used. FoamView was then used to extract statistical information from the foam. The methods used to get the statistical data from the foam were subject to human judgment and error, so the statistical results cannot be trusted with much confidence. Also, even though many of the features of the foam could clearly be seen in the 5% barium sulfate sample, there were still certain sections in the data set where the features were not well defined. The ill-defined sections in the data mean that the user has to make educated guesses about the structure of the foam in certain sections. The low resolution led to flaws in the images obtained from imaging and is the reason why only one pore of foam was analyzed using FoamView. If more pores were analyzed, the inaccuracies caused by manual measurement would have been compounded, making the data even less representative of the foam, however a reasonable histogram similar to a bell curve would have been able to be obtained. Even though the statistics produced by this one case using FoamView were not very useful, the exercise was still a success because it showed the types of information that can be gained once a better imaging data set is produced.

Future research

Although the barium sulfate sample did not produce data that was sufficiently detailed to create a 3D model with, it was promising enough that further research is warranted.

There are other common contrast agents that are used in the medical industry, such as iodine, that were not used in this experiment that could be tested for this application. There are also changes in the methods that can be tested, such as substituting latex or some other material for the agar, or heating the contrast agent to a higher temperature before pouring it over the foam samples.

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