ANAESTHESIA FLUID DETECTION IN 3D CONTRAST ENHANCED ULTRASOUND IMAGING

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Abstract - Ultrasound medical imaging system is frequently used in anaesthesiology, for example in navigation of a needle into certain part of human body and studying the spreading of the fluid inside the body. Some advantages of this medical imaging system are concerning the safety, good resolution, fast, and low operation cost. Ultrasound imaging system has a disadvantage concerning on displaying fluid area because it has low intensity. A contrast agent called microbubbles is introduced to enhance the intensity of the fluid. This microbubbles has high echogenicity which able to give more reflection on the fluid. Microbubbles are produced from the combination of liquid and gas which are not hazardous to the body. The size of microbubbles must be very small in order to be able to flow inside the blood vessels. After injecting the contrast agent inside the body, it is possible to develop a visualization of anaesthesia fluid spreading inside the body. The algorithm presented in here detects the anaesthesia fluid in each 2D plane and visualize the detected fluid into a 3D volume visualization.

Keywords : microbubbles, anaesthesia fluid detection, volume visualization, contrast enhanced ultrasound

I. INTRODUCTION

Ultrasound-based imaging system, or ultrasonography, has become an important part of anaesthesia procedure. It can display structure, needle, and surrounding tissue simultaneously, and allows a medical professional to observe the condition inside the scanned tissue area. However it has certain disadvantages on scanning low intensity area, especially when it used to study fluid inside the body.

Contrast agents are developed on helping the quality of imaging, but until recently, they had a little place in ultrasonography. This has chaned with the introduction of microbubbles; small gas filled bubbles. Microbubbles are produced from combination of liquid and gas not hazardous to the body. When they are inserted inside the body, it resonates in the ultrasound beam, rapidly contracting and expanding in response to the pressure changes of the sound wave. Therefore it is able to give more reflection on fluid area.

3D Transducer expands the possibilities on studying the spreading of anaesthesia fluid. 3D image consist of slices of 2D image on three different planes and a volume combination of the scanned slices. The fluid area will be most likely contained inside the scanned data set image. Therefore it is possible to present the anaesthesia fluid volume visualization.

II. ULTRASOUND IMAGING

2.1 Ultrasound

Ultrasound is a wave with high frequency, which is above the upper limit of human hearing. This audible sound is typically below 20 kHz [1].

Velocity

Velocity refers to how fast the disturbance passes from one particle to another. It is stated that the velocity of propagation of sound is constant in a certain medium. Therefore it can be concluded that velocity of sound will change according to the change of the medium it passes through. The higher the velocity of sound propagation is, the higher the intensity and brightness is.
Propagation velocity of some materials concerning to human inner organs and tissues are given in the following table [2]:

<table>
<thead>
<tr>
<th>Material</th>
<th>Velocity (m/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air</td>
<td>343</td>
</tr>
<tr>
<td>Fat</td>
<td>1410 – 1470</td>
</tr>
<tr>
<td>Water (20° – 37°)</td>
<td>1482 – 1523</td>
</tr>
<tr>
<td>Nerve tissue</td>
<td>1510</td>
</tr>
<tr>
<td>Soft tissue (average)</td>
<td>1540</td>
</tr>
<tr>
<td>Muscle</td>
<td>1545 - 1631</td>
</tr>
<tr>
<td>Blood</td>
<td>1570</td>
</tr>
<tr>
<td>Bone</td>
<td>2100 – 4080</td>
</tr>
<tr>
<td>Metal</td>
<td>3000 – 6000</td>
</tr>
</tbody>
</table>

Table 2.1 Table of propagation sound velocity in some biological materials

**Boundary behaviour**

There is a moment when sound travels through a medium and meets another medium with different characteristic impedance. There are some factors that influence the boundary behaviour:
- Difference characteristic impedance of two medium
- Orientation of sound beam towards the interface plane
- Surface of interface
- Distance between surface and sound source
- Frequency of the ultrasound wave

**2.2 Ultrasound in Medical Field**

Ultrasound imaging is relatively inexpensive and portable, comparing to other imaging techniques. An ultrasound wave is generated when an electric field is applied to an array of piezoelectric crystals located on the transducer surface. Strong, short electrical pulses from the ultrasound machine make the transducer ring at the desired frequency. The sound is focused either by the shape of transducer, lens in front of transducer, or a complex set of control pulses from the ultrasound machine. This focusing produce an arc-shaped sound wave where it travels into the body and comes into focus at desired depth [3].

![Figure 2.1 Sound wave emitted from Ultrasound Transducer](image)

There are two aspects that the sonographic scanner must determine from each received echo:
- How long it took the echo to be received from when the sound was transmitted
- How strong the echo was

The time it takes for the echo to travel back to the probe is measured and used to calculate the depth of the tissue. The greater the difference between acoustic impedances is, the larger the echo is. If it hits gases or solids, the density difference is so great that most of the acoustic energy is reflected and it becomes impossible to see deeper.

**2.3 3D Transducer**

Transducer is a device that converts energy from one to another form. In ultrasound machine, it is used to convert electrical energy into mechanical energy. Medical application use Brightness-mode for acquisition, where it will use brightness as the distinguisher on image. At first 2D transducer is used to produce 3D image by swiping the transducer in constant speed and direction. 3D image will be reconstructed in external software. This
provides more difficulties for real-time studying and diagnosing, thus the three-dimensional transducer later introduced for producing 3D and 4D images. It works in the same basic principal with 2D transducer, only that the waves are sent into the body at multiple different angles.

The image is generated from simultaneous reconstruction of two standard orthogonal 2D planes (X and Y), with the additional dimension of elevation. Using this type of image, one can see width, height, and depth of images without movement involved.

III. ULTRASOUND CONTRAST AGENT

Medical contrast medium or contrast agent is a substance used to enhance the contrast of structures of fluids within the body in medical imaging [4]. There are several types of contrast media used in medical imaging and they can roughly be classified based on the imaging method where they are used.

Ultrasound contrast agents rely on the different ways than the other contrast agents in which sound waves are reflected from interfaces between substances. These contrast agents might take a form of the surface of a liquid, containing small-encapsulated microbubbles, which very efficiently scatter ultrasound.

This contrast agent is formed from combination of certain liquid and gas. Not all combination of liquid and gas available to use for forming microbubbles because the contrast agents needs to dissolve inside the body without inflicting any harm effect on the body. Injecting a gas into the circulation may seem potentially hazardous, but the clinical studies show that tiny volume of air or gas given into the body is not dangerous.

Microbubbles structure generally divides into these categories [5]:

- **Microbubbles shell**
  
  Selection of shell material will determine how easily the microbubble is taken up by the immune system. A more hydrophilic material tends to be taken up easily, which reduces the life cycle in the circulation. This will reduces the time available for contrast imaging. The shell material also affects microbubble mechanical elasticity. Chosen liquid substance will affect on how long microbubbles last inside the body and how it will keep the gas from leaking out from microbubbles. The more elastic the material is, the more acoustic energy it can withstand before bursting. The shell also makes the bubble stiffer than a free gas bubble of equal size.

- **Microbubbles gas core**
  
  The gas core is the most important part of the ultrasound contrast microbubbles, because it determines the echogenicity.
When gas bubbles are caught in an ultrasonic frequency field, they compress, oscillate and reflect a characteristic echo where this will generate the strong and unique sonogram in contrast-enhanced ultrasound. Gas cores can be composed of air, or heavy gases like nitrogen or helium, because these gases are proven not to inflict any harmful effect when injected inside the body. Heavy gases are less water-soluble, thus making them less likely to leak out from the microbubble to impair echogenicity.

Choosing the combination of microbubble shell and gas core is very important because it has to be able to last longer inside the body and give no harmful effects. The ideal qualities of an ultrasound contrast agent require it to have high echogenicity, low attenuation, low blood solubility, and low diffusivity. Microbubbles have a tremendous difference in acoustic impedance as compared to surrounding fluid due to the large differences in density, elasticity, and compressibility, thus making gas bubbles have high degree of echogenicity, which is the ability of an object to reflect the ultrasound waves [5]. The echogenicity difference between the gas in microbubbles and the soft tissue surroundings of the body is immense. Therefore ultrasound imaging using microbubble contrast agent enhance reflection of the ultrasound waves, to produce a unique sonogram with increased contrast due to the high echogenicity difference.

Microbubbles are very useful for diagnosing blood or liquid flow using ultrasound because of the high difference of acoustic impedance at the interface between microbubbles and fluid substance.

**IV. PRODUCING MICROBUBBLES**

Commercial contrast agent are very expensive compared to the amount of microbubble comes with the price. Microbubbles are produced from chemical reaction between gas and liquid phase components catalysed by a solid. It is important to set a production system where it is possible to control size and numbers of microbubbles produced.

The production system will require a syringe system for pumping the liquid, a customized micro channel, and a tank filled of specified gas.

![Figure 4.1 System Set Up](image)

The liquid will be pumped by the syringe system with controllable flow rates while the gas is pumped from a tank controlled by the pressure valve on the tank and near the entrance of microchip channel. These two variables are the only controllable variable on the system, therefore the velocity and length of the produced bubbles, as well as numbers of bubbles produced, depends on these two variables.

![Figure 4.2 Cross-section channel and mixer formation](image)

The liquid is divided into two channels before it is mixed with gas flow. If the combination between the gas pressure value and liquid flow rate is correct, then the gas would be able to push through the liquid and produced gas bubble. It is not recommended to randomly choose liquid flow rate, since it has to consider the cross-sectional area of the channel and mixer and superficial liquid and gas velocity for specific flow to produce bubbles with temperature of 20°C and a pressure of 1 bar. The cross sectional area is 50 by 50 µm² while the superficial liquid and gas velocity for bubble flow is $10^3$ m/s respectively [6].
\[ Q_i = A_x U_i x U_g \]
\[ Q = 9 \text{ mL/h} \]

The value above is used as reference on producing microbubbles. The produced microbubbles must be the requirements as contrast agent. First the ultrasound machine must be able to detect the bubbles. Second, the bubbles must be stable and does not form bigger bubble when they are colliding. Using water and CO\(_2\) combination lead into an unstable microbubbles. Water doesn’t produce strong shell to hold gases from leaking out. There are some occasions when the bubbles collide to each other forming a bigger bubble in the end of the channel. In order to produce more stable bubbles, a physiological solution is introduced as the liquid. This liquid hopefully will create a stronger bubbles shell to encapsulate CO\(_2\) inside the bubble. Using Tween80 makes the system produce more stable and homogeneous microbubbles. These microbubbles do not easily shrink in size by the end of the channel and do not easily collide to form larger bubbles. This behaviour also proves that these bubbles have longer life cycle where they keep staying on the form of larger bubbles unless the container was shaken. Therefore this liquid provides to be successful solution for the production process.

Above is one of the experiment result with the combination of various flow rate between 7-10 mL/h and pressure rate of 1 bar. The length of produced bubbles is decreasing as the flow rate increasing because it will be difficult for the gas to go through high liquid flow rate. Whilst the numbers of bubble produced is increasing as the flow rate is increasing.

To see whether the produced microbubbles meet previous requirements, an experiment with ultrasound machine will be conducted. In order to prolong the life cycle of microbubbles once they were taken away from the output container, the microbubbles will be stored in Tween80 liquid inside a rubber container. A comparison has to be made in order to get exact result for the produced microbubbles. SonoVue is a well-known commercial ultrasound contrast agent developed by Bracco Diagnostic, Inc. It is designed to optimize the resistance to pressure. This contrast agent is filled with SF6, where it has low solubility and diffuses slowly in blood. It also has a high flexible shell, made from lipids, and very strongly echogenic in a wide range of frequencies and acoustic pressure.
The produced microbubbles used here is a combination of Tween80 0.1% as liquid and CO$_2$ as gas and the setting for production system are 20 mL/h for liquid flow rate and 1 bar for pressure rate. This setting will produce the smallest and stable microbubbles. From picture above, it can be seen that the ultrasound machine is able to detect the produced microbubbles. The reason why it is not as bright as SonoVue is because the amount of produced microbubbles is fewer than SonoVue. The shell of produced microbubbles also doesn’t have similar strength in echogenicity, considering it is only coated by liquid, while another layer for more protection coats SonoVue.

This experiments use a medium level of mechanical index, where it give no destructive effect to the bubbles. The bubbles give no changing effect on the behaviour. To see whether the produced bubble have a good resistance against the high level of mechanical index, the transducer will produce high frequency signal called Flash. If after applying Flash mode and there is almost no change to the microbubbles, then they are stable.

The picture above contains graphs explaining about the intensity value on specified regions of interests of Tween80 0.1% microbubbles ultrasound image in the order of time. The sudden peak in intensity value explains the power of Flash mode.

On the graphs above, the intensity value of the produced microbubbles before and after applying Flash mode are similar. Therefore it is possible to extract result that the produced microbubbles is stable.

V. ANESTHESIA FLUID VOLUME VISUALIZATION

To present the fluid area visible in the image, contrast agent must be injected first inside the body. Then in the ultrasound image, there will be bright area, which is where the anaesthesia fluid is. The experiment will use a model that resembles human tissue, called tissue-mimicking phantom.

The acquired 3D image must be segmented into 2D image plane where only sagittal plane will be processed further. The algorithm will detect the fluid area in each 2D plane and then present the detected fluid area into 3D volume visualization.

5.1 Data Normalization

Each image data acquired from an ultrasound machine will have a different range of intensity with different variations. The data quality depends on the patient’s condition and the characteristic of the contrast agents.

Since the region of interest in image is high intensity area, some unwanted data (low intensity objects) can be removed or reduced by doing data normalization. Data normalization will use statistical distribution, where a mean ($\mu$) is the data average value while standard deviation ($\sigma$) represents the spread of the data around the mean. The fluid area in the body always has intensity more than the standard deviation from its mean ($\mu+\sigma$) because the mean of the 3D data itself is quite low. Therefore
this value \((\mu + \sigma)\) can be used to extract a certain range of data intensity where the fluid area separates from the background.

\[
\text{roi} = data - (\text{mean} + \text{std})
\]

This is one of the original image slices acquire from ultrasound machine. The brightest area in the image is where the contrast agents are focused. The formula for data normalization will eliminate most of the unwanted area on the image.

5.2 Edge Detection
Due to data normalization applied to the image slices, it is possible that the fluid area is no longer complete. It is important to mark the extracted fluid area and restore it to original size and shape. The best solution for the algorithm is to detect the border of the area.

Canny approximation method find edges by looking for local maxima of the gradient of the image. The gradient is calculated using the derivative of a Gaussian filter. This method uses two thresholds, high and low threshold, to detect strong and weak edge and includes the weak edges in the output only if they are connected to strong edges.

It will be able to detect the weak extracted edge of the fluid area \([7]\).

When greyscale data is converted into black and white version, a threshold is used to divide data into foreground and background. The intensity value of each voxel is compared to the threshold. If it is higher, then it will be turned to white.

5.3 Morphological Operation

The result in edge detection returns an image where only lines of edge available in the image. The fluid area itself is still not completely returned. Therefore, the algorithm needs to fill the holes between the edges to return the fluid area into original shape.

There are many structuring elements available in MATLAB. Since the edge is lines with many possible directions within 3D data, two lines of SE are used for the image where it can trace the edges and dilate them.

After dilating the image, the fluid area is almost return back to its original size and shape. The result still contains black areas inside the fluid area due to its low intensity. There is a function to fill those holes in order to show a black and white image of the completed fluid area. This operation will detect the holes first by comparing the
surrounding value and add more pixels to the area.

Figure 5.5 Detected Fluid Area

In this picture, the fluid area is completely detected and presented in black and white version after comparing to the original image.

5.4 Fluid Volume Visualization

Volume visualisation is the creation of graphical representations of data sets that are defined on three-dimensional grips [8]. The algorithm will segment 2D image planes into 3D view before connecting the outer edges of each fluid area and presenting it into 3D volume visualization.

Figure 5.1 Volume Visualization

VI. CONCLUSION AND RECOMMENDATION

6.1 Conclusion

- 3D scanning provides more possibility to visualize volume data set on anaesthesia fluid.
- Ultrasound has obvious disadvantage on displaying low intensity area, such as fat, blood, and anaesthesia fluid. Ultrasound contrast agent, created to handle this problem, is a small gas filled bubbles.
- Microbubbles is produced from chemical reaction between liquid and gas. There are two important variable for producing microbubbles: liquid flowrate and gas pressure rate.
- The produced microbubbles has slight disadvantage against commercial microbubbles on its echogenicity because the commercial one is protected with another layer.
- The manipulated data in here is 3D data set where it has more complexity than 2D data and requires more computational time. However, since most of the detection method requires 2D image, it first needs to simplify the 3D data into 2D.
- The algorithm will detect fluid area in each 2D images and then visualize into 3D volume.

6.2 Recommendation

- The production system needs to be more advance where it can produce more microbubbles and portable. Therefore the microbubbles can be directly inserted into the patient while producing them.
- The experiments should use more variety in Tween80 concentration and gas substance to see the effects to the produced contrast agents, especially on its acoustic behaviour.
- It will be very useful to emerge the volume visualization with the original image to see exactly where the anaesthesia fluid located in the image.

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Sylmina Dalily Alkaff was born in Surabaya, August 4th, 1988. She is the only daughter of Prof Abdullah Alkaff and Elly Purwantini. After graduated from SMUN 6 Surabaya in 2006, she continue her study in Electrical Engineering Department, Faculty of Industrial Technology, Institute Technology of Sepuluh Nopember Surabaya. During her study in ITS, she decided to concentrate on control system engineering. On her last year in ITS, she got a chance to finish her last year in Netherland as double degree student. She is accepted in Fontys Hogescholen, Eindhoven, and study in Mechatronics. Her graduation project is done in Catharina Ziekenhuis, Eindhoven. On June 14th, she is declared as graduated student in Fontys Hogescholen, thus also earning her second degree in ITS automatically.