Examination of Cerebral Aneurysm by Scanning Acoustic Microscopy

Bukem Tanoren (bukem.bilen1@boun.edu.tr)
Bogazici University

Research article

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Examination of Cerebral Aneurysm by Scanning Acoustic Microscopy

Bukem Tanoren

Bogazici University, Department of Physics, Istanbul, Turkey

bukem.bilen1@boun.edu.tr

ORCID: 0000-0001-7992-0501

Abstract

Background: Asymptomatic intracranial aneurysms rupture without any warning, therefore, use of high-resolution imaging techniques for the rupture risk assessment is essential.

Methods: This study's goal is to assess the feasibility of scanning acoustic microscopy (SAM) in the characterization of cerebral aneurysm. The aneurysm's dome samples were obtained from 12 different patients with and without subarachnoid hemorrhage.

Results: The acoustic impedance values are found statistically higher in samples from female patients than in samples from male patients. On the other hand, sample from a male patient without subarachnoid hemorrhage has higher acoustic impedance value when compared with samples from male patients with subarachnoid hemorrhage, however, this discrepancy is not observed in female patients.

Conclusion: In summary, the success of SAM in monitoring the altering acoustic impedance values in male and female patients with and without subarachnoid hemorrhage indicates the potential of SAM for the diagnosis of instability of cerebral aneurysms.

Keywords

Scanning acoustic microscopy, cerebral aneurysm, acoustic impedance, subarachnoid hemorrhage

Abbreviations

Scanning acoustic microscopy	SAM
Brain magnetic resonance imaging	MRI
Computed tomography angiography	CTA
Digital subtraction angiography	DSA
Magnetic resonance angiography	MRA
Optical coherence tomography	OCT
Acoustic impedance	AI

Declarations

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Conflicts of interest/Competing interests The author declares that she has no conflict of interest.

Ethics approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki and its later amendments or comparable ethical standards. The study was approved by the Ethics Committee of Biruni University.

Consent to participate Written informed consent was obtained from all individual participants included in the study.

Consent for publication Informed consent was obtained from all individual participants included in the study.

Availability of data and material The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Code availability Not applicable.

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Introduction

Dilations of blood vessels within the brain are called cerebral aneurysms. At major branch points in the Circle of Willis [1], weakening of media wall cause cerebral aneurysms and their rupture causes subarachnoid hemorrhage [2] associated with high mortality rates, therefore, diagnosis and definitive treatment of cerebral aneurysms, before or very shortly after rupture, are crucial. Treatment is done either with clipping or coiling [3] and aneurysm exclusion is evaluated with angiography, which includes contrast agent injection and can only reveal vessel shape. On the other hand, healing of treated aneurysms has to be followed and currently, there are no modalities available in clinics for visualization of healing process with sufficient resolution. These disabilities urge many researchers to develop new imaging techniques.

Brain magnetic resonance imaging (MRI) is a frequently used in the diagnosis of intracranial hemorrhage. Monitoring methods such as computed tomography angiography (CTA), digital subtraction angiography (DSA) and magnetic resonance angiography (MRA) are used in cranial vascular pathologies [4, 5]. Even though, these angiographic methods provide high accuracy results, they

have advantages and disadvantages over each other. MRA uses intravenous contrast agents and repeated ionizing radiation exposure for producing a high-resolution image. The gold standard method for the detection of intracranial aneurysms is DSA but it is an expensive modality. On the other hand, CTA is cheaper and also non-invasive when compared to DSA. Optical coherence tomography (OCT) endovascular catheter reveals the vessel wall structure with a high resolution, providing information for the assessment of the vessel healing progress [6], however, flushing of blood is necessary for a good OCT signal. Scanning acoustic microscopy (SAM) will be an alternative to these investigation tools. SAM can supply morphological and mechanical information simultaneously, with micro-meter level resolution. Ultrasound signals are used to define the elastic properties of biological tissues by calculating sound speed through tissues [7-9] or acoustic impedance of the tissues [10]. When compared with the techniques previously mentioned, SAM has the advantage of micro-meter level resolution, the capability of non-destructive monitoring, no requirement of a special sampling, the ability of quick measurement (less than 2 minutes for a 4.8 mm x 4.8 mm area) [11] and the applicability to tissues [12-15] or cell populations [16-20]. Besides, a SAM probe would enable its use in clinics [21].

Here, we reported the first application of SAM system, equipped with an 80 MHz transducer, offering a lateral resolution of approximately 20 μm, for the characterization of cerebral aneurysm's dome samples. For this purpose, acoustic impedance mode of SAM was used and the acoustic impedance values of the specimen were recorded. The findings indicate that SAM can resolve variations in samples of male and female with and without subarachnoid hemorrhage, therefore, for the quantitative assessment of life-threatening aneurysms in clinics SAM is a promising tool, offering benefits of micro-meter level resolution by

preserving sample's integrity, non-destructive and easy-to-perform mechanism and rapid measurement.

Materials and Methods

Specimens

This study was ethically approved by Biruni University Ethics Committee and informed consent was obtained from each participant. Aneurysm's dome samples were obtained after microsurgical clipping. Briefly, standard pterional craniotomy was performed and the aneurysm was exposed by opening the Sylvian fissure and gradually dissecting the originating vessel. After establishing proximal and distal control, the aneurysm's neck was dissected and a permanent clip was placed. Following the clip ligation, the aneurysm's dome was dissected from surrounding tissue and cut as close to the clip as possible. Immediately after removal, the dome was preserved in 4 % formaldehyde solution for SAM studies.

Scanning Acoustic Microscopy

The methods were carried out in accordance with Bogazici University Institutional Review Board for Research with Human Subjects. The aneurysm's dome tissues were examined by scanning acoustic microscope (AMS-50SI) built by Honda Electronics (Toyohashi, Japan). Fig. 1 shows acoustic impedance (AI) mode schematic of SAM setup. A transducer with a quartz lens, a pulser/receiver, an oscilloscope, a computer with a display monitor constitute SAM setup. The spot size of 80 MHz transducer is 17 μm and its focal length is 1.5 mm. It is a pulser/receiver, since it collects the reflected acoustic waves as well as sending them. Distilled water is the coupler the quartz lens and the substrate. For two-dimensional scanning of the transducer, there is an X-Y stage. The signals,

reflected from the reference and also the target material, are analyzed by the oscilloscope. Finally, the maps of acoustic intensity and impedance with a lateral resolution of approximately 20 μm are visualized with 300 x 300 sampling points.

The signal reflected from the target material in Fig. 1 is

$$S_{target} = \frac{Z_{target} - Z_{sub}}{Z_{target} + Z_{sub}} S_0 \quad (1)$$

where, S_0 is the signal transducer generates, Z_{target} is target material's acoustic impedance and Z_{sub} is the polystyrene substrate's acoustic impedance (2.37 MRayl). The signal reflected from the reference is

$$S_{ref} = \frac{Z_{ref} - Z_{sub}}{Z_{ref} + Z_{sub}} S_0 \quad (2)$$

where, Z_{ref} is the acoustic impedance of distilled water (1.50 MRayl). Then, acoustic impedance of the target under investigation is given as

$$Z_{target} = \frac{1 + \frac{S_{target}}{S_0}}{1 - \frac{S_{target}}{S_0}} Z_{sub} \quad (3)$$

with a constant signal S_0 [19], transducer generates.

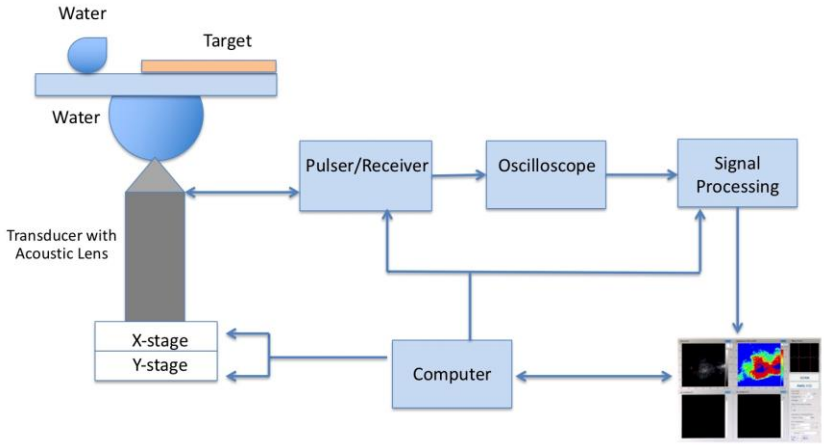

Fig. 1. AI mode schematic of SAM. The signals reflected from water and the aneurysm's dome sample surfaces are combined for the acoustic impedance value calculation of the tissue.

Results

Aneurysm's dome samples received from patients were very thin, therefore like two-dimensional structures with plain facets, and were examined by using AI mode. Fig. 2 shows the acoustic impedance map of a male aneurysm's dome sample. This map was constructed by collecting the ultrasound signals reflected from reference (water) surface and the aneurysm's dome sample surface on the polystyrene substrate. As can be seen in Fig. 2, acoustic impedance is smaller than 2 MRayl. Table 1 presents average acoustic impedance values of all dome samples studied in this investigation.

Table 1. Average acoustic impedance values of aneurysm's dome samples of male and female patients with and without subarachnoid hemorrhage. 6 female and 6 male patients were studied for the correlation of gender and hemorrhage on the dome sample.

Gender	Acoustic Impedance (MRayl)	Hemorrhage
Male	1.853 ± 0.061	Yes
Male	1.821 ± 0.049	Yes
Male	1.850 ± 0.083	Yes
Male	1.890 ± 0.022	Yes
Male	1.893 ± 0.039	Yes
Male	2.007 ± 0.031	No

Female	1.943 ± 0.032	Yes
Female	2.093 ± 0.018	Yes
Female	2.030 ± 0.031	Yes
Female	2.068 ± 0.019	Yes
Female	2.041 ± 0.024	Yes
Female	2.027 ± 0.024	No

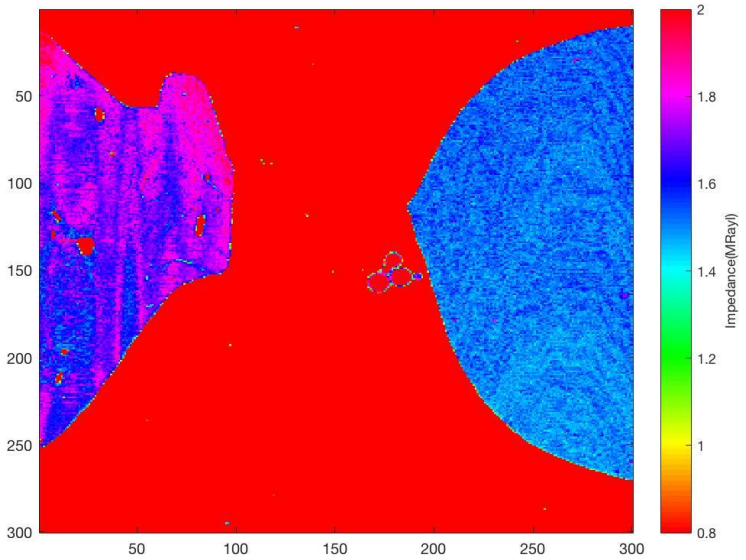

Fig. 2. Acoustic impedance map of a male aneurysm's dome sample, obtained by comparing the reflected ultrasound signals from the surfaces of water and the dome sample, with 300 x 300 sampling points, in a scanning area of 4.8 mm x 4.8 mm. Distilled water droplet, which has the acoustic impedance of 1.5 MRayl, is more homogeneous shape on the right.

Discussion

We have shown that SAM can characterize aneurysm's dome samples by the calculation of the acoustic impedance. The acoustic impedance values are

calculated to be higher for all female patients' samples with and without subarachnoid hemorrhage when compared to male patients' samples with subarachnoid hemorrhage, indicating gender dependence on the contents of aneurysm's dome samples. Age interval of the patients is chosen quite narrow, between 50 and 60, and almost all of the patients have hemorrhage, only 1 male and 1 female have no subarachnoid hemorrhage. We assume that these observations are due to parameters like gender or lifestyles, which influence aneurysm development. The higher acoustic impedance value is observed a result of higher elastic modulus. Aneurysm dome samples of female patients with and without subarachnoid hemorrhage are firmer and therefore easily distinguishable. On the other hand, there is no significant discrepancy in acoustic impedance values of dome samples of female patients with and without subarachnoid hemorrhage, which is an indication of no hemorrhage dependence in female patients. In male patients' samples, hemorrhage has an effect on acoustic impedance, in other words, on elasticity, therefore, samples with hemorrhage, which are softer tissues, have lower acoustic impedance values.

All of aneurysm's dome samples, received from female and male patients, were firmer than normal vessel tissue, however, in this study, we only studied samples with or without hemorrhage but not a normal vessel tissue sample, therefore, we were unable to compare our results with a reference. 6 male and 6 female patients with and without subarachnoid hemorrhage were studied for the correlation of gender and hemorrhage on dome samples. Two-dimensional maps, as in Fig. 2, are acquired with micro-meter level resolution and average acoustic impedances are calculated. As can be seen in Table 1, dome sample of male patient without a subarachnoid hemorrhage, has the highest acoustic impedance value, when compared with those of other male patients. In other words, almost all patients had hemorrhage which are detected due to symptoms like severe headache or

nausea, patients have just after hemorrhage starts. Brain aneurysms below 4 mm are not detectable with conventional imaging methods and when aneurysm is more than 7 mm [22], it is more likely to rupture causing subarachnoid hemorrhage, which may take place at any time. Ruptured aneurysms are closely related to mortality and morbidity. Therefore, discrimination of dome samples of male patients with and without subarachnoid hemorrhage by SAM is an indicator of the feasibility of this modality in the diagnosis of aneurysms prone to rupture in clinics.

Conclusion

Here, we present the capability of SAM in characterizing the cerebral aneurysm's dome samples for the first time. Acoustic impedance maps of the tissues display distinctive values in male and female patients. On the other hand, hemorrhage has an apparent effect on samples of male patients, while there is no significant difference in female patients' samples. Consequently, we can say that SAM has a potential as an imaging tool in clinics and will be able to do rupture risk assessment, since it can acquire information about the morphology and elasticity of the samples. However, first, SAM has to be developed on a probe for direct evaluation of vessel wall structure during surgeries.

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Figures

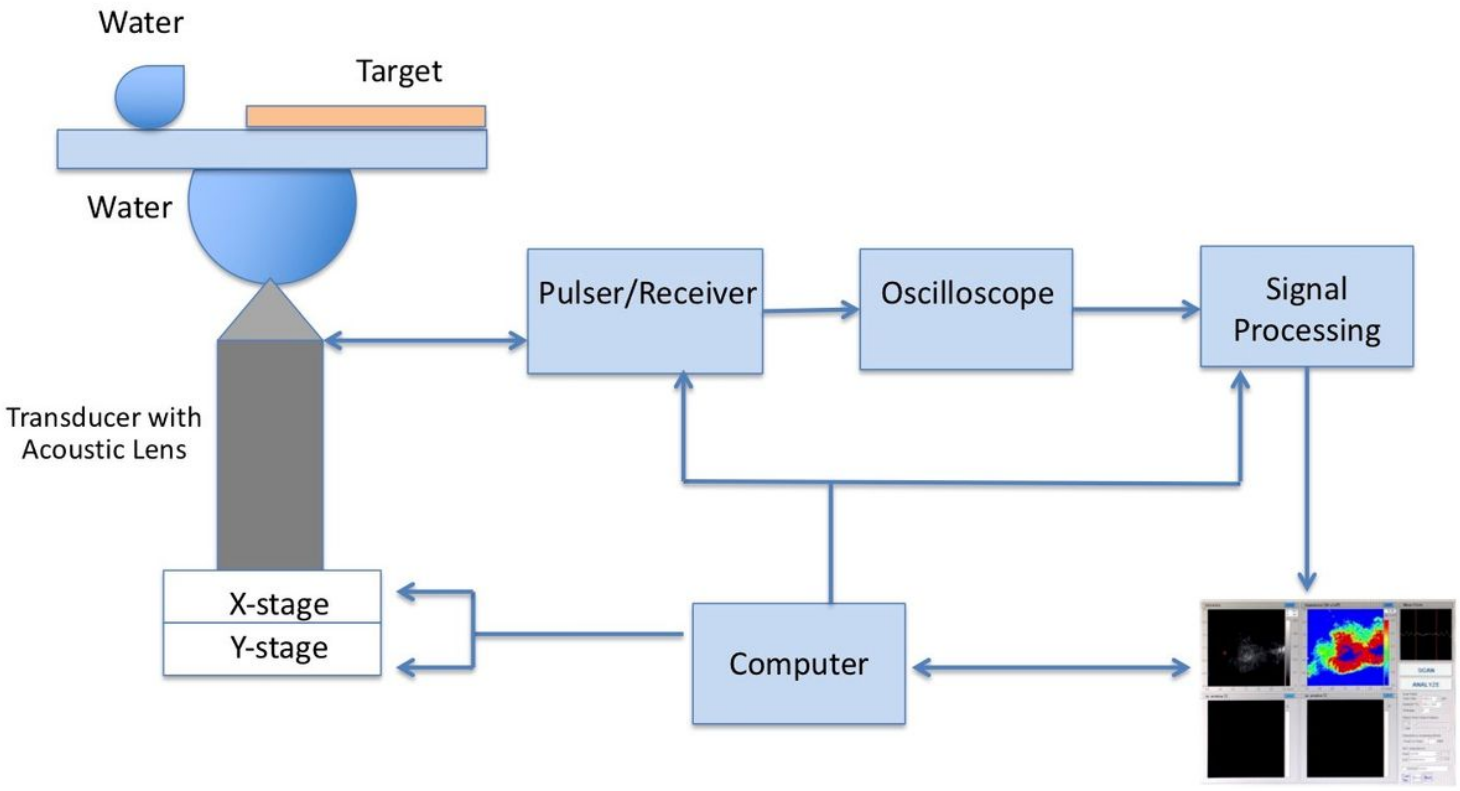

Figure 1

AI mode schematic of SAM. The signals reflected from water and the aneurysm's dome sample surfaces are combined for the acoustic impedance value calculation of the tissue.

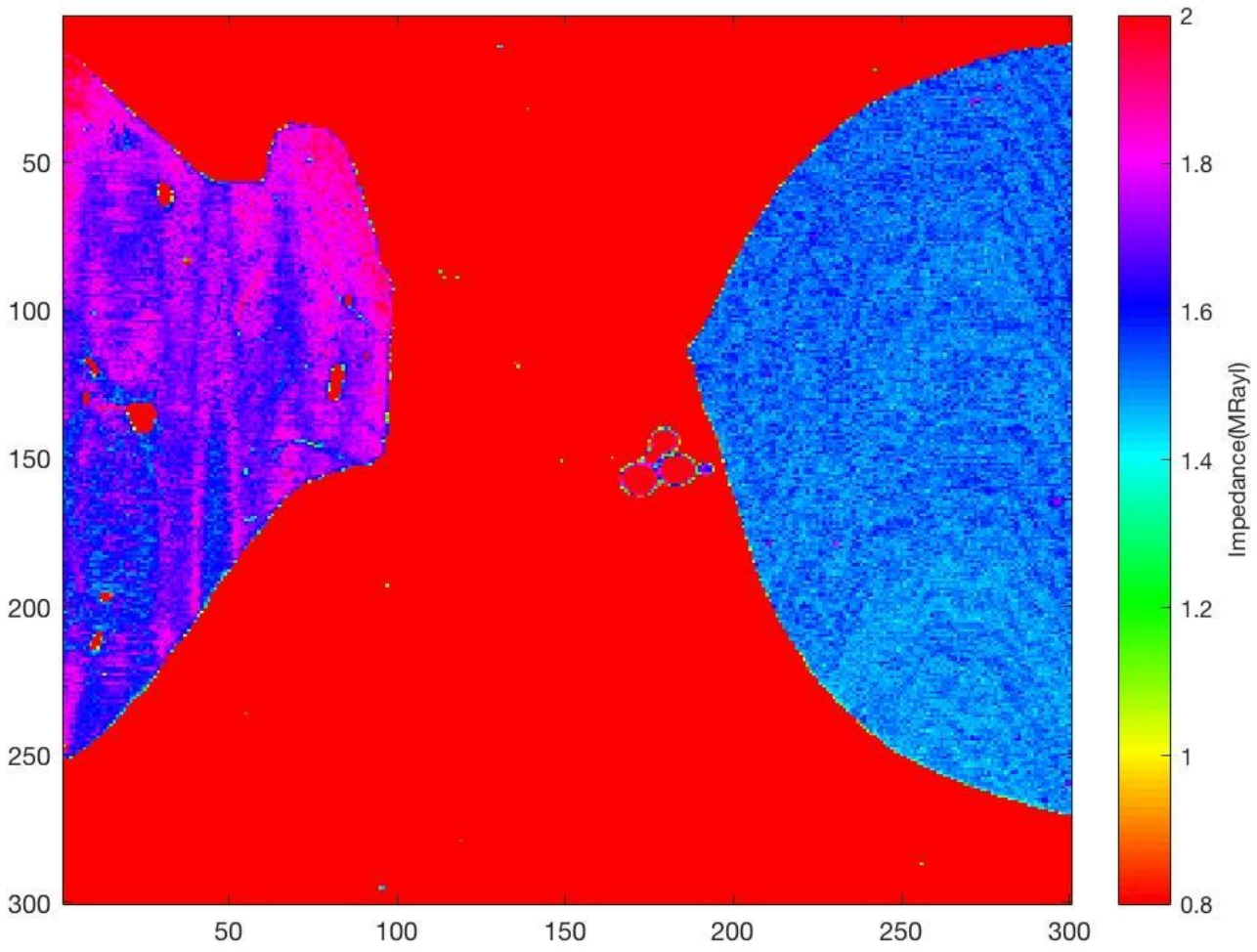

Figure 2

Acoustic impedance map of a male aneurysm's dome sample, obtained by comparing the reflected ultrasound signals from the surfaces of water and the dome sample, with 300 x 300 sampling points, in a scanning area of 4.8 mm x 4.8 mm. Distilled water droplet, which has the acoustic impedance of 1.5 MRayl, is more homogeneous shape on the right.