別紙４（課程博士）

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| Department 電気・電子情報学専攻 | Student ID Number 学籍番号 | 第 129202 号 |
|---|---|---|
| Applicant's name 氏名 | Agus Indra Gunawan | |

| Supervisors 指導教員 | Naohiro Hozumi<br>Yoji Sakurai<br>Masayuki Nagao |
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**Abstract**

# 論文内容の要旨　(博士)

| Title of Thesis 博士学位論文名 | A Study on Acoustic Impedance Microscopy for Biological and Medical Applications (生物･医療応用のための音響インピーダンス顕微鏡に関する研究) |
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(Approx. 800 words)
(要旨　1,200 字程度)


This study deals with a new type of biological acoustic microscopy to indicate acoustic impedance of biological soft tissues and cells. The system is a scanning acoustic microscope (SAM) that can obtain two-dimensional (2D) image of acoustic property by scanning the region of interest.

Acoustic impedance microscopy has been proposed since several years ago. A soft biological tissue is placed on a polymer substrate and an ultrasound beam in the frequency range of 30 - 100 MHz focused onto the interface is transmitted through the substrate. The reflection intensity is normalized by that from the reference material placed in the same condition as the target and interpreted into the cross-sectional characteristic acoustic impedance of the target. Mechanical scan with a microscale precision makes it possible to produce 2D acoustic impedance image. This research is mainly aimed to realize a precise calibration for interpreting the response signal into the absolute value of acoustic impedance.

In the conventional observation system, an acoustic transducer with a small angle of focusing was employed. In such a case, all beam components could be assumed to be perpendicular to the interface (vertical incidence) when the reflection was interpreted into acoustic impedance. The interpretation used to be done by considering simple simultaneous equations. However, as the beam was poorly focused, the spatial resolution (in the lateral direction) was not sufficient.

Herewith, we proposed improvement method for the conventional system. A transducer with a large focus angle of focusing (22o in half aperture angle) was used instead of the previous transducer. Fourier analysis was employed to analyze and decompose the beam components. Acoustic intensity was calculated by considering sound field distribution. Based on this calculation, we establish a calibration curve, which precisely converts acoustic intensity into acoustic impedance. To verify the calibration curve, saline solutions with several contents of which acoustic impedance were known were observed by the same system. The measurement results were then plotted on the same chart as the analytical result. There was a good agreement between calculation and measurement results. As an experimental work, we observe cerebella

r tissue of a rat. The layers of the cerebellar tissue were clearly observed with the absolute value of characteristic acoustic impedance which can be c orrelated with the elastic property.

In the second part of the study, we tried to access a cultured cell. Several adjustment and analysis were done, because some stuff in the previous syst em were no longer compatible. Since the target was much smaller than tiss ue scale, a sapphire lens transducer with a frequency range spreading from 200-400 MHz was used. A new calibration curve for cell size observation w as established by considering all acoustic propagation in the lens, coupling medium and substrate. The measurements of several saline solutions were p erformed for verification. A good agreement was seen between calculation an d measurement results. As an experimental work, we observed cultured glia and investigated the difference in the effect of anticancer drug onto glia a nd glioma cells.

In the third part of the study, utilizing the above system, we tried to acces s the internal structure of a cultured cell. It was realized by focusing the a coustic beam onto the cell and receive the reflection from the substrate plac ed behind the cell. As an experimental work, we observed cultured glia and glioma cells. We compared the observation results of cell in terms of acous tic impedance and internal structure. It was shown that this mode of obse rvation can see internal structure of the cell including the nucleus. Whereas the acoustic impedance mode can mainly see the cross-sectional (interfacial) property of the target. In addition, we also investigate the structure of sm eared hepatoma cells.

Through these three parts of this study, two advantages have been clarified. Observation can be finished in a very short time because this observation may skip staining process, which is usually required in the case of optical o bservation. Since the observation can be performed introducing no contamin ant and invasion to the biological system, it is highly advantageous for med ical and biological applications.