3J2-4

Non-invasive measurement of temperature elevation inside tumor tissue of living rat induced by radiofrequency current heating based on statistical analysis of ultrasonic scattered echoes

超音波散乱波統計解析によるラジオ波加熱されたラット腫瘍組織内温度上昇の非侵襲測定

Michio Takeuchi[1,5†], Toshihiko Sakai[1], Gabor Andocs[2,3], Keizo Takao[4,5], Ryo Nagaoka[6], and Hideyuki Hasegawa[6] ([1]Tateyama Kagaku Industry Co., Ltd.; [2]Tateyama Machine Co., Ltd.; [3]Dept. of Radiological Sciences, Grad. School of Medicine and Pharmaceutical Sciences, Univ. of Toyama; [4]Dept. of Behavioral Physiology, Grad. School of Medicine and Pharmaceutical Sciences, Univ. of Toyama; [5]Div. of Animal Resources and Development, Life Science Research Center, Univ. of Toyama; [6]Grad. School of Science and Engineering for Research, Univ. of Toyama)

竹内道雄 [1,5†]，坂井俊彦 [1]，Andocs Gabor[2,3]，高雄啓三 [4,5]，長岡　亮 [6]，長谷川英之 [6] ([1] 立山科学工業, [2] 立山マシン, [3] 富山大学大学院医学薬学研究部（医学系）放射線基礎医学講座, [4] 富山大学大学院医学薬学教育部（医学系）行動生理学講座, [5] 富山大学研究推進機構研究推進総合支援センター生命科学先端研究支援ユニット, [6] 富山大学大学院理工学研究部）

1. Introduction

Non-invasive measurement of internal body temperature distribution has a huge potential for the medical field. Especially, temperature distribution inside human body is considerable information for carrying out oncological hyperthermia therapy safe, correctly, and effectively. Temperature distribution of human body is desired to be measured during hyperthermia treatment. However, the current situation of the treatment is that the therapy is conducted without monitoring internal body temperature including temperature of malignant tumor tissue in almost all cases. Because there is no realistic method to non-invasively detect internal body temperature distribution during heating under the therapy. A realistic method to non-invasively measure temperature distribution inside human body is demanded in the oncological hyperthermia societies for three decades.

In this decade, a promising novel acoustic method for non-invasive measurement of internal body temperature was proposed by some research groups.[1,2)] They found out that some statistical parameters obtained from ultrasonic scattered echoes can be an indicator of temperature variation inside biological tissue specimens. Our research group has been also focusing on its possibilities of non-invasively monitoring temperature distribution inside human body with temperature dependence of the Nakagami shape parameter m for oncological hyperthermia treatment. We previously reported phantom and ex vivo study results.[3,4)] In this study, we present an in vivo study result that a temperature elevation inside a tumor tissue of a living rat induced with radiofrequency (RF) current heating was detected by statistical analysis of ultrasonic scattered echoes.

2. Specimen and method

In this study, we prepared a 9L (glioma) cell line derived heterotopic tumor tissue grown around the joint of the hind-limb of a Slc:SD female rat. The tumor tissue was heated from 35.5 up to 42.5 °C by passing RF current at the frequency f = 13.56 MHz between two electrodes holding the rat's hind-limb including the tumor tissue. Reference temperatures were measured by flexible fiber optic temperature sensor probes and temperature measurement system (Luxtron m3300). Some fiber optic temperature sensor probes were inserted into the tumor tissue. In this study, we use temperatures measured at the central region of the tumor tissue as a reference temperature. Ultrasonic echoes scattered from the induced tumor tissue were measured using an ultrasonic measurement system (Microsonic RSYS0002) with a linear array transducer (Hitachi UST-5412). The experimental setup is shown in Fig. 1(a). And a close-up photo around the tumor tissue is shown in Fig. 1(b). All procedures for animal experiments were approved by the Institutional Animal Care and Use Committee at University of Toyama (A2017OPR-2).

†m-take@tateyama.or.jp

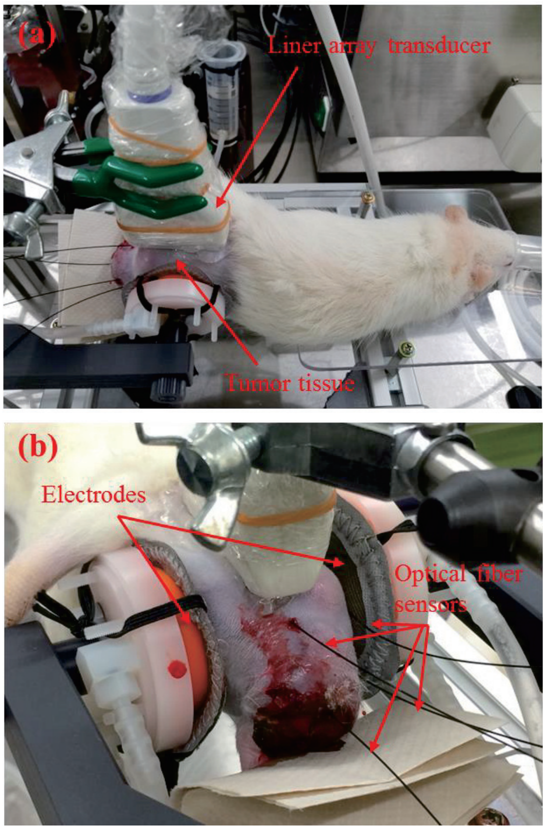

Fig. 1. (a) Experimental setup. (b) Close-up photo.

3. Analysis and discussion

In signal processing, analytic signals were elicited by applying Hilbert transformation to measured ultrasonic RF signals, and the envelope signals were obtained. Moreover, the histograms of envelopes in each region of interest (ROI) was created for statistical analysis. The Nakagami shape parameter m was obtained by fitting the Nakagami distribution function to the histogram of the envelope of the ultrasonic scattered echoes. In this study, the statistical analysis was carried out by setting ROI size at 0.6×0.6 mm^2.

In order to express temperature changes inside tumor tissue, a specific parameter $\alpha_{\mathrm{mod.}}$ that indicates absolute values of ratio changes of m values was calculated using the following equation

$$\alpha_{\mathrm{mod.}} = \left|\gamma \cdot \log_{10}\left(\frac{m_T}{m_{T_R}}\right)\right|, \qquad (1)$$

where m_{TR} and m_T are the Nakagami shape parameter m at a baseline temperature and each temperature, and γ denotes the multiplying factor. In our previous study,[4] it was shown that the magnitude of the change in the Nakagami shape parameter m due to a temperature rise has a dependence on the initial m-value at a baseline temperature. Therefore, the ratio changes of m values were amplified based on the initial m-values by the multiplying factor γ varying as a function of the initial m-value. The multiplying factor γ was defined to be proportional to m^{-1}.

The hot-scale images indicating absolute values of ratio changes of m values, $\alpha_{\mathrm{mod.}}$, estimated with the baseline temperature T_{R} = 35.5 °C are shown in Fig. 2. In the hot-scale images, overall increase in brightness with increasing temperature was clearly observed. The increase in brightness is assumed to imply a temperature elevation in the tumor tissue.

4. Conclusion

It was observed that the internal temperature of tumor tissue increased with rising reference temperature in the hot-scale images. The result shows that our acoustic method is expected to be a useful modality of monitoring internal body temperature for hyperthermia therapy.

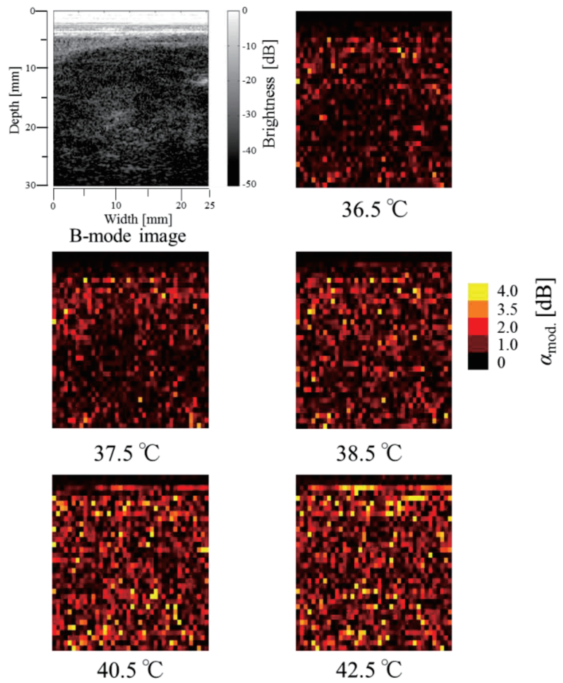

Fig. 2. B-mode image and hot-scale images indicating absolute value of ratio changes of m values, $\alpha_{\mathrm{mod.}}$ for tumor tissue.

References

1. P.-H. Tsui, Y.-C. Shu, W.-S. Chen, H.-L. Liu, I.-T. Hsiao, and Y.-T. Chien, Med. Phys. **39**, 2369 (2012).
2. M. Byra, E. Kruglenko, B. Gambin, and A. Nowicki, Acta Phys. Pol. A **131**, 1525 (2017).
3. M. Takeuchi, Y. Matsui, T. Doi, Y. Takano, G. Andocs, and H. Hasegawa, Jpn. J. Appl. Phys. **57**, 07LB17 (2018).
4. M. Takeuchi, Y. Matsui, T. Sakai, G. Andocs, R. Nagaoka, and H. Hasegawa, Jpn. J. Appl. Phys. **58**, SGGE09 (2019).