Tissue-Mimicking Phantom Useful in Simulating Laser Light-Tissue Interactions

Keun Jae Ahn¹
Beom Joon Kim²
Sung Bin Cho^{2,3}

¹Department of Science Education, Jeju National University, Jeju, Korea

²Department of Dermatology, Chung-Ang University Hospital, College of Medicine, Chung-Ang University, Seoul, Korea

³Kangskin Sillim Dermatology Clinic, Seoul, Korea

Significant methodological advancements in preclinical experiments using Schlieren imaging, *in vitro* cell lines, *ex vivo* tissues, human cadaver tissues, and tissue-mimicking (TM) phantoms have been tremendously helpful in outlining actual skin reactions to laser or light energy. Polyacrylamide hydrogel TM phantom containing bovine serum albumin, with some modifications, depending on the study design, can be used to simulate laser- or light-induced tissue reactions. Although experiments in TM phantoms do not mirror *in vivo* laser light-induced skin reactions exactly, mainly due to the lack of cellular components and adnexal structures, TM phantoms are useful in determining which devices and settings offer better treatment results and safer delivery of laser energy to experimental and clinical subjects.

Key words

Laser; Tissue-mimicking phantom; Laser-tissue interaction; Q-switched neodymium-doped yttrium aluminum garnet laser; Long-pulsed alexandrite laser; High-intensity focused ultrasound

Received November 21, 2015

Revised November 23, 2015

Accepted November 24, 2015

Correspondence

Sung Bin Cho
Department of Dermatology, Chung-Ang University Hospital, 102 Heukseok-ro, Dongjak-gu, Seoul 06973, Korea
Tel: +82-2-6299-3081
Fax: +82-2-811-1159
E-mail: drsbcho@gmail.com

© Korean Society for Laser Medicine and Surgery

© This is an open access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Laser- or light-based therapeutic devices are continually introduced for the treatment of dermatologic disorders. However, experimental results of laser light-tissue interactions achieved when using such devices are limited by the lack of standardized guidelines and regulations, as well as ethical problems with the use of animal and human test subjects. Recently, significant methodological advancements in schlieren imaging, *in vitro* cell lines, *ex vivo* tissues, human cadaver tissues, and tissue-mimicking (TM) phantoms have helped with visualizing actual skin reactions to laser or light energy. Although these methods are not without limitations, preclinical study data can help practitioners and investigators better predict macro- and microscopic tissue reactions for various laser- or light-based therapeutic devices.

For example, our study group recently reported the geometric patterns of thermal injury zone (TIZ) formation upon high-intensity focused ultrasound (HIFU) treatment of TM phantom composed of bovine serum albumin and polyacrylamide hydrogel.¹ In our previous study of HIFU-tissue interactions, 9% (w/v) bovine serum albumin was added as a temperature-sensitive indicator to the standard TM phantom.¹ In the study, focused acoustic energy from five different HIFU devices was delivered to the TM phantom at focal penetration depths of 3 mm and 4.5 mm and at low power settings of 0.45–1.2 J.¹ Then, digital photographs were taken to measure the mean heights and widths of the TIZs using image processing software.¹ In the study, HIFU-induced TIZs and the patterns of thermal injury varied for each device.¹

The standard TM phantom is made from an optically transparent polyacrylamide hydrogel and bovine serum albumin, which works as a temperature-sensitive indicator.² Additionally, by adding higher acrylamide concentrations, the attenuation coefficients can be heightened, compared to biologic tissues or standard TM phantom.² For specific experimental purposes, a suspension of glass beads can be added to obtain a backscatter coefficient: Choi et al.² proposed that the use of a bovine serum albumin and polyacrylamide hydrogel-based TM phantom containing glass beads more accurately predicts HIFU-induced tissue reactions, as it more closely mimics the acoustics of human and animal tissue.

Recently, we have conducted experiments, the results of which have yet to be published, to simulate the effects of Q-switched and long-pulsed lasers under various settings on tattoo ink embedded in TM phantom. To do so, we added 5% (w/v) bovine serum albumin, rather than 3%, 7%, and 9%, to the standard TM phantom for better visualization of the photoacoustic effects of the lasers on the

tattoo ink and surrounding TM phantom. To develop the tattoo pigment-TM phantom, a 30-gauge, 2.5-mm long needle attached to a 1-ml syringe was utilized to inject approximately 0.02 ml of tattoo ink into the TM phantom. In this experimental setting, treatment of the ink particles with a Q-switched 1,064-nm neodymium-doped yttrium aluminum garnet (Nd:YAG) laser or long-pulsed 755-nm alexandrite laser resulted in various photoacoustic tissue reactions (Fig. 1A). Among the many laser-tattoo interactions, tissue vacuolization was readily noted, which is difficult to observe in *in vivo* tissue samples due to the rapid dissolution of plasma or gas into the surrounding tissue (data not published).

Maxwell et al.³ demonstrated that HIFU-induced cavitation can be visualized using agarose hydrogel TM phantom supplemented with red blood cells (RBCs). In their study, RBC-agarose TM phantom was prepared by solidifying agarose phantom, pouring RBCs onto the agarose phantom, allowing it to solidify again, and finally, pouring agarose solution onto the RBCs-suspended agarose phantom.³ Additionally, in order to simulate interactions between laser energy and hair shafts, our study group also developed a hair shaft-embedded bovine serum al-

Fig. 1. Examples of simulated laser light-tissue interactions using tissue-mimicking (TM) phantom. (A) Long-pulsed 755-nm alexandrite laser treatment on a tattoo pigment-TM phantom with polyacrylamide hydrogel and 5% (w/v) bovine serum albumin. The tattoo ink-embedded phantoms were treated at a fluence of 35 J/cm², a spot size of 6 mm, and a pulse duration of 5 msec. (B) Long-pulsed 755-nm alexandrite laser treatment on a hair shaft-embedded TM phantom. The hair shaft-embedded phantoms were treated at a fluence of 30 J/cm², a spot size of 12 mm, and a pulse duration of 3 msec.

bumin and polyacrylamide hydrogel-based TM phantom. To do so, TM phantom was prepared by mixing polyacrylamide hydrogel and 5% (w/v) bovine serum albumin in distilled water. After degassing and polymerization, the final mixture was poured into a rectangular polycarbonate housing, and plucked hairs were inserted in the mixed solution before it solidified. On the hair shaft-embedded TM phantom, Q-switched 1,064-nm Nd:YAG or long-pulsed 755-nm alexandrite laser treatment was applied and resulted in various photoacoustic tissue reactions on the hair shaft and surrounding tissues (Fig. 1B).

Due to the lack of cellular components and adnexal structures, TM phantoms do not exactly mirror *in vivo* laser light-induced skin reactions. However, we believe that TM phantoms are useful in evaluating which laser devices and settings offer the best treatment results and facilitate the safest delivery of laser energy to experimental and clinical subjects. Further investigations should be conducted to establish standardized guidelines for using schlieren imaging, *in vitro* cell lines, *ex vivo* tissues, human cadaver tissues, and TM phantoms in preclinical evaluations of newly developed laser- or light-based devices.

ACKNOWLEDGMENTS

We would like to thank Anthony Thomas Milliken, ELS (Editing Synthese, Seoul, Korea) for his help with the editing of this manuscript.

REFERENCES

1. Kim HJ, Kim HG, Zheng Z, Park HJ, Yoon JH, Oh W, et al. Coagulation and ablation patterns of high-intensity focused ultrasound on a tissue-mimicking phantom and cadaveric skin. *Lasers Med Sci* 2015;30:2251-8.
2. Choi MJ, Guntur SR, Lee KI, Paeng DG, Coleman A. A tissue mimicking polyacrylamide hydrogel phantom for visualizing thermal lesions generated by high intensity focused ultrasound. *Ultrasound Med Biol* 2013;39:439-48.
3. Maxwell AD, Wang TY, Yuan L, Duryea AP, Xu Z, Cain CA. A tissue phantom for visualization and measurement of ultrasound-induced cavitation damage. *Ultrasound Med Biol* 2010;36:2132-43.