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Photoacoustic Characterization of Radiofrequency Ablation Lesions

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Abstract

Radiofrequency ablation (RFA) procedures are used to destroy abnormal electrical pathways in the heart that can cause cardiac arrhythmias. Current methods relying on fluoroscopy, echocardiography and electrical conduction mapping are unable to accurately assess ablation lesion size. In an effort to better visualize RFA lesions, photoacoustic (PA) and ultrasonic (US) imaging were utilized to obtain co-registered images of ablated porcine cardiac tissue. The left ventricular free wall of fresh (i.e., never frozen) porcine hearts was harvested within 24 hours of the animals' sacrifice. A THERMOCOOL[®] Ablation System (Biosense Webster, Inc.) operating at 40 W for 30-60 s was used to induce lesions through the endocardial and epicardial walls of the cardiac samples. Following lesion creation, the ablated tissue samples were placed in 25 °C saline to allow for multi-wavelength PA imaging. Samples were imaged with a Vevo[®] 2100 ultrasound system (VisualSonics, Inc.) using a modified 20-MHz array that could provide laser irradiation to the sample from a pulsed tunable laser (Newport Corp.) to allow for co-registered photoacoustic-ultrasound (PAUS) imaging. PA imaging was conducted from 750-1064 nm, with a surface fluence of approximately 15 mJ/cm² maintained during imaging. In this preliminary study with PA imaging, the ablated region could be well visualized on the surface of the sample, with contrasts of 6-10 dB achieved at 750 nm. Although imaging penetration depth is a concern, PA imaging shows promise in being able to reliably visualize RF ablation lesions.

Keywords

photoacoustic imaging; radiofrequency catheter ablation; cardiac arrhythmias; lesion imaging

1. INTRODUCTION

Atrial fibrillation (AF) is the most common cardiac arrhythmia observed in clinical practice^(1, 2). It has been shown that as AF continues, electrical and structural remodeling occur in the left atrium⁽²⁾. This remodeling helps sustain an arrhythmia, making AF a progressive disease⁽²⁾. AF is also a major factor in several diseases, including stroke, coronary artery disease and sudden cardiac death and has a demonstrated role in increasing

medical care costs associated with cardiovascular pathologies^(3, 4). For these reasons, AF has a significant impact on public health and has become an active area of medical research.

Firing from ectopic foci, typically located in the pulmonary veins, has been observed as a common source of AF^(1, 2). Effective electrical isolation of these arrhythmogenic foci is the most common treatment for AF after anti-arrhythmic drugs have failed⁽⁵⁾. Radiofrequency ablation (RFA) has become the preferred method for achieving this electrical isolation⁽⁵⁾. RFA treats an arrhythmia through the creation of non-conductive lesions within the myocardium with the application of radiofrequency energy, commonly applied on the endocardial surface, via a catheter introduced percutaneously through the femoral vein^(1, 5, 6). Proper lesion contiguity and transmuralit is critical to effectively block arrhythmogenic wavefronts^(1, 5, 6). The current standard of care uses several imaging systems to assist the procedure. Intercardiac echocardiography and fluoroscopy are used to determine catheter placement and orientation, but they lack the soft tissue contrast needed to accurately characterize lesion boundaries^(7, 8). Electrical measurements made during the procedure with a coarse electro-anatomical mapping system can determine conduction blockage at the location of the catheter tip, but assessment of lesion contiguity and transmuralit is difficult with such a technique⁽⁸⁾. An inability to accurately visualize lesion boundaries contributes to the high rate of treatment failure and the need for costly repeat procedures. It has been suggested that treatment outcomes will not significantly improve until a real-time lesion monitoring method is introduced, allowing for an adaptive RFA treatment plan⁽⁵⁾.

The photoacoustic (PA) effect describes the phenomenon whereby light energy is absorbed by a substance and converted into an acoustic pressure wave by thermoelastic expansion^(9, 10). This pressure wave can be detected and imaged with a traditional ultrasound (US) imaging system^(9, 10). PA imaging is capable of noninvasively probing the optical absorption properties of tissue. When the length of the irradiating light pulse is sufficiently short, the emitted pressure wave peak can be modeled as

$$P_0 \propto \Gamma \cdot F \cdot \mu_a, \text{ where } \Gamma = \frac{\beta \cdot c^2}{c_p},$$

where Γ is the Grüneisen coefficient, μ_a is the wavelength-dependent absorption coefficient, F is the optical fluence, β is the thermal coefficient of volume expansion, c is the speed of sound in the given medium, and C_p is the heat capacity at constant pressure^(9, 10). The above relationship highlights several possibilities for the use of PA imaging in medicine. It demonstrates that PA contrast may be seen between materials with different absorption coefficients. It also suggests that the temperature dependence of parameters such as β , c and C_p may be used to quantify the temperature of tissue. Research has already demonstrated the possibility of temperature monitoring using PA for thermal cancer therapy⁽⁹⁾.

Previous studies have shown that the optical properties differ between thermally ablated versus native bovine and porcine myocardium^(11, 12). In particular, the absorption coefficient of ablated myocardium has been measured to increase by 50-100% over that of untreated

(i.e., non-ablated) tissue^(11, 12). Since peak pressure is dependent upon μ_a , this suggests that PA imaging may be capable of differentiating ablated versus non-ablated tissue. By imaging lesions post-ablation in a constant temperature water bath, we can account for the temperature dependence of β , c and C_p . As a result, after normalizing for variations in surface fluence, we expect the generated PA signal to depend solely on tissue specific parameters.

2. METHODS

Four fresh porcine hearts were acquired (Sierra Medical Inc.) within 24 hours of being harvested. The left ventricular free wall was excised, and the tissue samples were transported on ice to the clinical site where ablation took place. During ablation, the samples were placed in saline to allow for electrical coupling between the ablation catheter, the tissue sample and the dispersive electrode. RFA was performed using a Stockert 70 RF generator (Biosense Webster Inc.) and a THERMOCOOL[®] irrigated tip catheter (Biosense Webster Inc.) flushed by a COOLFLOW[®] pump (Biosense Webster Inc.). Following common clinical practice, during the application of RF energy the catheter was flushed with 30 mL/min of saline. The RF generator was set to output 40 W, and RF energy was applied for durations of 30 to 60 seconds by a trained electrophysiologist.

Multiple lesions were generated on both the epicardial and endocardial surfaces of the sample. Immediately following the final application of RF energy on a given sample, the sample was placed back into a sealed bag on ice. After all of the samples had been ablated, they were transported to the imaging facility. At the imaging facility, the ablated area was dissected into roughly 4 cm × 2 cm × 2 cm squares, in which the lesion was centrally located.

Imaging was achieved with a modified Vevo[®] 2100 (VisualSonics Inc.) ultrasound (US) system that is capable of PA imaging (Fig. 1). Laser irradiation was provided by a Quanta-Ray pulsed Nd:YAG laser with a premiScan tunable OPO (Newport Corp.). The laser had a 5-ns pulse width and provided a surface fluence of approximately 15 mJ/cm² for all wavelengths utilized. Most lesions were imaged at 750 nm, while one lesion was spectroscopically imaged from 750 to 1020 nm in 30-nm increments and at 1064 nm. Roughly 5% of the laser energy was deflected by a beam splitter and measured with an optical power meter to allow for fluence normalization. Light delivery was accomplished by coupling the irradiation source to the sample with a fiber optic bundle. A custom housing was used to attach the fiber bundle to the US transducer face so that laser irradiation was coincident with the US insonification. A 256-element linear array transducer, operating at 21 MHz, was used to image the samples. Samples were positioned such that the US beam was perpendicular to the lesion and the myocardial surface. A mechanical system was used to translate the transducer and housing elevationally to allow for 3D imaging. The system was synchronized to allow for co-registration of B-mode and PA images (i.e., PAUS images).

Samples were placed in room temperature saline to be acoustically coupled with the US transducer. Sample cubes were scanned from edge to edge at a given wavelength. After imaging, a given sample was returned to a sealed plastic bag on ice until imaging of all of

the samples was completed. Following the completion of imaging (approximately 2 hours in duration), the samples were photographed overhead and then bisected and photographed again. To confirm lesion boundary delineation, histology was performed on one subset of samples. A bath of nitro blue tetrazolium (NBT), which has been shown to differentiate viable from non-viable myocardial tissue, was prepared⁽¹³⁾. An ablated sample was bisected mid-lesion and incubated at 35 °C for 20 minutes in the NBT bath. For comparison, an equivalently sized non-ablated control sample was also incubated at 35 °C for 20 minutes in the NBT bath.

Cross-sectional PAUS images were formed by summing the PA signal across the approximate lateral extent of the lesion, while C-scan images were generated by summing the PA signal across the approximate depth of the lesion. PAUS images were created by overlaying a PA image onto a co-registered B-mode image; regions in the PA image below a fixed threshold were not displayed to allow for B-mode visualization of the surrounding anatomy. PA signals are shown on a linear scale, while US signals are presented on a logarithmic scale. Additionally, contrast values were calculated as

$$\text{Contrast} = 20 \times \log_{10} \frac{\overline{S}_l - \overline{S}_b}{\overline{S}_b},$$

where $\overline{S}_l$ and $\overline{S}_b$ are the mean PA signals from equally sized regions within the lesion and adjacent background, respectively.

3. RESULTS

PA images from two representative lesions – one on the endocardial and one on the epicardial surface – are presented. In Fig. 2, photographs of a cross-section after bisection (a) and an overhead view before bisection (c) are offered for an endocardial lesion; matched PAUS or PA images are provided to the right of each photograph. In both photographs (a & c), the ablated region of myocardium can be seen a pale black-gray region, while non-ablated tissue is visible as the remaining red-pink regions. An increase in the PA signal emanating from the lesion's surface is apparent; PA images yield a lesion contrast (ablated to non-ablated tissue) of 6 dB. In the cross-sectional image (b), the increase in the PA signal is limited to superficial regions of the lesion and does not extend to the deep portions (approximately 18 mm) of the lesion. In the overhead image (d), PA signal is visible through the entire circumference of the lesion boundary.

In Fig. 3, photographs of a cross-section after bisection (a & b) and overhead before bisection (d & e) are offered for an epicardial lesion; a matched PAUS or PA image is provided to the far right of each photograph. The lesion boundaries denoted by the NBT stain (b & e) are similar to the boundaries indicated by the sample before staining (a & d). Much like results from the endocardial ablation, the PA signal is limited to the superficial region of the lesion (Fig. c). PA images yield a contrast (ablated to non-ablated tissue) of 10 dB. Pulse surface fluences were approximately 15 mJ/cm² (750 nm) for both experiments.

Figure 4 offers multi-wavelength analysis from 750 to 1064 nm. The normalized (i.e., to the surface fluence at a respective wavelength and to the maximum PA signal) PA signal tends to decrease with increasing wavelength; a slight local increase in the PA signal is observed at 1020 and 1064 nm. An approximate 50% reduction in PA signal was noted across the measured spectral range.

4. CONCLUSIONS

In this preliminary investigation, PA imaging offers contrasts of up to 10 dB of ablated versus native myocardial tissue. Additionally, the PA signal generation from the surface of the lesion correlates well with photographs of the lesion surface boundaries delineated in both stained and non-stained samples. Despite appreciable PA signal contrast observed at the surface, however, no significant PA signal contrast was observed beyond the superficial region of the lesion. Possible explanations for the superficial nature of the observed PA signal is that local fluence attenuates too rapidly through the ablated myocardial tissue to generate a significant PA signal at greater depths. Another explanation is that blood coagulate charring, which occurs exclusively at the catheter-tissue interface, may provide the actual source of PA signal contrast (i.e., this charred region provides increased optical absorption).

When considering the normalized PA signal as a function of optical wavelength, we see a trend of increasing signal at lower wavelengths (i.e., at higher energies). Previous work observed increases in optical absorption of ablated over native tissue when irradiating with 700 nm as opposed to 850 nm⁽¹²⁾. An even more significant increase (nearly threefold) in absorption of ablated over native tissue has been documented from 1150 nm to 1300 nm⁽¹¹⁾. This region shows promise as greater light penetration is generally possible at longer wavelengths, which may help alleviate the superficial nature of the PA signal generation seen in this study. In future studies, the range for multi-wavelength imaging will be increased to include these higher wavelengths. Additionally, increased pulse energies, up to the 100 mJ/cm² ANSI limit for skin⁽¹⁴⁾, will be utilized in an attempt to increase the local fluence achieved at the distal margins of the lesion.

In the event that a significant PA signal cannot be achieved beyond the surface of the lesion (e.g., in the case that contrast originates from charring), it could be possible to use PA imaging to monitor ablation therapy by other means. For example, PA imaging may have further potential in providing a tool to accurately measure tissue temperature in real time. Current standard of care utilizes impedance measurements at the distal catheter electrode to infer tissue temperature during the ablation. These measurements can correlate poorly with sub-surface tissue temperature as the endocardial surface is convectively cooled by blood flow. An inaccurate assessment of tissue temperature may lead to increased occurrences of a “steam pop.” In such a situation, a portion of the tissue is heated sufficiently to produce a pocket of steam that may then rupture and damage the myocardial surface, resulting in severe complications. PA-based techniques have demonstrated the ability to quantify tissue temperature during thermal therapy by utilizing the temperature dependence of the Grüneisen parameter⁽⁹⁾. Once the temperature dependent behavior of the Grüneisen parameter of myocardium is determined, PA imaging may be able to provide accurate, real-

time quantification of the temperature of myocardial tissue during an ablation procedure. Such a tool may improve a procedure's outcome by reducing the severity and frequency of steam pop complications and by providing a more thorough tool to assess lesion boundary based on a temperature threshold.

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REFERENCES

1. Haissaguerre M, Jais P, Shah DC, Takahashi A, Hocini M, Quiniou G, Garrigue S, Le Mouroux A, Le Metayer P, Clementy J. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *New England Journal of Medicine*. 1998; 339(10):659–666. [PubMed: 9725923]
2. Nattel S, Burstein B, Dobrev D. Atrial remodeling and atrial fibrillation. *Circulation: Arrhythmia and Electrophysiology*. 2008; 1(1):62–73. [PubMed: 19808395]
3. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke*. 1991; 22(8):983–988. [PubMed: 1866765]
4. Wolf PA, Mitchell JB, Baker CS, Kannel WB, D'Agostino RB. Impact of atrial fibrillation on mortality, stroke, and medical costs. *Archives of internal medicine*. 1998; 158(3):229. [PubMed: 9472202]
5. Shah D. A critical appraisal of cardiac ablation technology for catheter-based treatment of atrial fibrillation. *Expert Reviews of Medical Devices*. 2011; 8(1):49–55. [PubMed: 21158540]
6. Di Biase L, Burkhardt JD, Mohanty P, Sanchez J, Mohanty S, Horton R, Gallinghouse GJ, Bailey SM, Zagrodzky JD, Santangel P, Hao S, Hongo R, Beheiry S, Themistoclakis S, Bonso A, Rossill A, Corrado A, Raviele A, Al-Ahmad A, Wang P, Cummings JE, Schweikert RA, Pelargonio G, Dello Russo A, Casella M, Santarelli P, Lewis WR, Natale A. Left atrial appendage: an underrecognized trigger site of atrial fibrillation. *Circulation*. 2010; 122:109–118. [PubMed: 20606120]
7. Kanj M, Wazni O, Natale A. Pulmonary vein antrum isolation. *Heart Rhythm*. 2007; 4(3):73–79.
8. Gepstein L, Evans SJ. Electroanatomical mapping of the heart: basic concepts and implications for the treatment of cardiac arrhythmias. *Pacing and clinical electrophysiology*. 1998; 21(6):1268–1278. [PubMed: 9633070]
9. Shah J, Park S, Aglyamov S, Larson T, Ma L, Sokolov K, Johnston K, Milner T, Emelianov SY. Photoacoustic imaging and temperature measurement for photothermal cancer therapy. *Journal of Biomedical Optics*. 2008; 13(3):1–9.
10. Wang LV. Photoacoustic imaging and spectroscopy. CRC. 2009
11. Schwarzmaier HJ, Yaroslavsky AN, Terenji A, Willmann S, Yaroslavsky IV, Kahn T. Changes in the optical properties of laser-coagulated and thermally coagulated bovine myocardium. *SPIE*. 1998; 3254:361–365.
12. Swartling J, Palsson S, Platonov P, Olsson SB, Andersson-Engels S. Changes in tissue optical properties due to radio-frequency ablation of myocardium. *Medical & Biological Engineering & Computing*. 2003; 41(4):403–409. [PubMed: 12892362]
13. Thyer IA, Kovoov P, Barry MA, Pouliopoulos J, Ross DL, Thiagalingam A. Protection of the coronary arteries during epicardial radiofrequency ablation with intracoronary chilled saline irrigation: assessment in an in vitro model. *Journal of cardiovascular electrophysiology*. 2006; 17(5):544–549. [PubMed: 16684031]
14. American National Standards Institute. American national standard for safe use of lasers. ANSI Z136.1-2007. 2007

Figure 1. Diagram of the imaging system setup

Figure 2. Cross-sectional photograph (a), PAUS image (b), overhead photograph (c) and PA image (d) of an endocardial lesion. The cyan box in the photographs defines the field of view (FOV) for the associated PA image. In all PAUS images, a PA signal threshold was chosen to allow for visualization of the background ultrasound B-mode image

Figure 3. Cross-sectional photographs (a – no stain; b – NBT stain), PAUS image (c), overhead photograph (d – no stain; e – NBT stain) and overhead PA image (f) of an epicardial lesion. The cyan box in the photographs defines FOV for the associated PA image; no cyan box is provided for the cross-sectional images as sample boundaries are evident from the provided PAUS image

Figure 4. PA signal in lesion as a function of laser wavelength. Note that the PA signal is normalized to both surface fluence and the peak PA signal