Non-invasive Assessment of Tissue Heating During Cardiac Radiofrequency Ablation Using MRI Thermography

Running title: Kolandaivelu et al.; MRI Thermography of Cardiac Ablation

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Abstract:

**Background:** Failure to achieve properly localized, permanent tissue destruction is a common cause of arrhythmia recurrence following cardiac ablation. Current methods of assessing lesion size and location during cardiac radiofrequency ablation are unreliable or not suited for repeated assessment during the procedure. MRI thermography could be used to delineate permanent ablation lesions because tissue heating above 50°C is the cause of permanent tissue destruction during radiofrequency ablation. However, image artifacts caused by cardiac motion, the ablation electrode, and radiofrequency ablation currently pose a challenge to MRI thermography in the heart. In this study we sought to demonstrate the feasibility of MRI thermography during cardiac ablation.

**Methods and Results:** A MRI-compatible electrophysiology catheter and filtered RF ablation system was used to perform ablation in the left ventricle of six mongrel dogs in a 1.5T MRI system. Fast gradient-echo imaging was performed prior to and during RF ablation and thermography images were derived from the pre-heating and post-heating images. Lesion extent by thermography was within 20% of the gross pathology lesion.

**Conclusions:** MR thermography appears to be a promising technique for monitoring lesion formation and may allow for more accurate placement and titration of ablation, possibly reducing arrhythmia recurrences.

**Key words:** ablation, electrophysiology, imaging, magnetic resonance imaging
Introduction:

Catheter-based radiofrequency (RF) ablation creates circumscribed regions of myocardial necrosis that are used to interrupt reentrant pathways or block foci of automaticity. Ablation techniques are available to treat the majority of tachyarrhythmias including anatomically complex arrhythmias such as atrial fibrillation and monomorphic ventricular tachycardia. However, current techniques for determining the location and size of ablation lesions are unreliable. X-ray fluoroscopy with or without electro-anatomic mapping is the most common method of catheter guidance during EP procedures but is unable to visualize the soft tissue changes caused by ablation. Indirect parameters such as RF power, impedance, electrode temperature, and local electrogram changes are also poor at predicting lesion extent because of the variable influence of blood flow around the electrode and electrode/tissue contact. The poor ability to predict permanent lesion extent is important because ablation procedures can be prolonged and commonly fail because of improper lesion positioning and incomplete lesion generation.

RF ablation lesions are caused by thermal tissue damage. Permanent damage occurs in myocardium heated above 50°C for several seconds. Proton resonance frequency shift thermography (PRFST) is an MRI technique that can quantify the tissue temperature changes that lead to ablation lesion formation. The technique has been used to monitor ablation caused by many thermal energy sources, including RF energy, in a number of organs including the liver, prostate, and uterus.
Cardiac PRFST has not been reported because of the imaging difficulties posed by heart motion.\textsuperscript{10} This study demonstrates that PRFST visualization of myocardial heating during RF ablation is possible using motion artifact reduction techniques.

\textbf{Methods:}

The PRFST Method

The temperature sensitivity of the proton resonance frequency (PRF) was described by Hindman in 1966.\textsuperscript{11} The PRF temperature dependence of pure water, -0.01 part per million (ppm) per °C, appears constant over a wide temperature range from -15 to +100°C.\textsuperscript{11} A number of in-vitro and in-vivo calibration experiments have since been performed on various animal and human tissues. Most report a temperature dependence of the PRF of between -0.009 and -0.01 ppm/°C, similar to the pure water value, for non-fat tissues including muscle.\textsuperscript{12} This temperature dependence does not appear to change significantly after tissue is thermally coagulated.\textsuperscript{13}

The PRF temperature dependence was first adapted for imaging by Ishihara in 1995.\textsuperscript{14} Change in local PRF between pre-heating and post-heating states can be detected as a regional phase difference between pre-heating and post-heating gradient recalled echo (GRE) phase images. This can be translated into regional temperature change maps using the relationship:

$$\Delta T(\Delta \phi) = \frac{\Delta \phi}{\gamma B_0 \alpha TE} \quad (\text{Equation 1})$$
Where $\Delta T$ is the temperature change in °C, $\Delta \phi$ is the pixel phase difference between images (in radians), $\gamma$ is the proton gyromagnetic ratio ($2\pi \times 42.58$ MHz/Tesla), $B_0$ is the static magnetic field (in Tesla), $\alpha$ is the temperature dependence of the PRF shift (in ppm/°C), and TE is the GRE imaging sequence echo time in seconds.

The optimal TE to maximize the phase difference signal to noise ratio (SNR) is the tissue $T_2^*$ parameter. The $T_2^*$ for muscle tissue is around 40ms. However, when cardiac GRE imaging is performed with a TE of 40ms, significant imaging artifacts result from motion over the TE periods as illustrated in Figure 1A. We found that a TE of around 9ms maximized TE while providing sufficiently small motion artifact. (Figure 1B)

In a 1.5Telsa scanner using a TE of 9ms and $\alpha$ of -0.010 ppm/°C for muscle tissue, the relationship in Equation 1 simplifies to:

$$\Delta T(\Delta \phi) = (-27.69^{\circ}C/\text{rad}) \Delta \phi \quad (\text{Equation 2})$$

In-vitro Validation

To assess the ability of the proposed PRFST technique to detect a range of tissue temperature changes, the following in-vitro test was performed. A 7F MRI compatible copper electrode catheter was used for ablation. Five 1 to 2cm thick sections of beef left ventricle (LV) were suspended on a vertically oriented platform. The ablation electrode contacted the tissue from one side and a fiber-optic temperature probe (Luxtron FOT Lab...
Kit, LumaSense Technologies, Santa Clara, CA) was inserted from the opposite side to a depth of around 10mm. The assembly was placed in a temperature regulated saline bath held at 37 degrees using an in-line pump (Little Giant, Oklahoma City, OK), water heater (Bosch, Waitsfield, VT), and temperature feedback controller (Acqualogic, San Diego, CA). Imaging was performed in a 1.5 Tesla MRI scanner (Espree, Siemens Medical Systems, Erlangen, Germany) using standard chest matrix and spine array coils. A standard RF generator (Atakr I, Medtronic, Minneapolis, MN), with additional 10MHz low pass and 64MHz choke filtering to suppress image artifacts, was used for ablation in the MRI scanner. An ECG generator (214A Patient Simulator, DNI Nevada, Carson City, NV) provided a simulated cardiac gating signal at 80 beats per minute.

High-resolution GRE imaging, slice thickness 1.5mm, identified an imaging plane through the ablation electrode and fiber-optic temperature probe tip. Three cardiac gated GRE images were then obtained before ablation. Imaging parameters were the same as used for the animal study: flip angle=25 degrees, TE=9ms, TR=91ms, 6=segments/TR, FOV=220x165mm, resolution=128x96, slice thickness=4mm, and averages=2. External saline irrigation of the ablation electrode, delivered through a supporting sheath at 15 to 20ml/min, was started prior to ablation to provide surface cooling. RF power was then titrated until the tissue temperature recorded by the fiber-optic probe was stable at 45°C +/- 1°C. Two to three images were then acquired during continued RF application. RF power was then titrated to tissue temperatures of 50, 60, 70, 80, and 90°C +/- 1°C or until maximum RF output or high impedance was reached. Imaging was repeated during continued RF application at each temperature level. Thermography image processing
was performed as described in the thermography image generation section below. The fiber-optic probe temperature was compared to the tissue temperature determined by thermography using linear regression. The closest thermography value within a 1 acquired pixel area (0.85mm radius) and a 2.5 acquired pixel area (1.4mm radius) of the fiber-optic probe tip location was used for regression analysis.

Animal Preparation and Experimental Protocol

All animal protocols were reviewed and approved by the Animal Care and Use Committee at the Johns Hopkins University and conformed to the guidelines published in the “Position of the American Heart Association on Research Animal Use.”

Six mongrel dogs (63 to 75 lbs.) were studied during mechanical ventilation under isoflurane general anesthesia. Using fluoroscopy guidance, a 35cm 9F sheath was inserted into the left ventricle (LV) through a carotid artery and the same copper electrode catheter used in the in-vitro study was positioned against the mid antero-septal wall.

The animals were transferred to a 1.5 Tesla MRI scanner (Espree, Siemens Medical Systems, Erlangen, Germany). Metoprolol and/or amiodarone were administered intravenously (IV) to achieve a heart rate of 90 to 115 bpm. Standard True-FISP imaging was used to identify an imaging plane through the electrode tip for subsequent temperature imaging. In different animals, different imaging orientations through the electrode were selected to identify the optimal plane for lesion visualization.
The same RF generator, filtering system, imaging coils, and cardiac gated GRE imaging sequence used for the in-vitro study was used for the animal study. Three cardiac gated, diastolic, breath-hold GRE images were obtained before ablation. The same GRE imaging was then performed as RF power was increased in 3W increments until an electrode temperature 80°C and then 1W increments until high impedance was reached. The images during ablation were obtained 30 seconds to one minute after changes in RF power when stabilization of the temperature reading from the electrode temperature sensor was noted. In four animals, images were also obtained 60 seconds after stopping RF power at an electrode temperature of 60°C. The time required for each image collection was 10 to 20 seconds depending on the heart rate.

Delayed gadolinium-enhanced MRI (DEMRI) is a validated technique for assessing ablation lesion size using MRI.\textsuperscript{16} After thermography imaging, Gadolinium 0.2mg/lb was administered intravenously and cardiac gated, diastolic, breath-hold, phase sensitive inversion recovery DEMRI was performed 60 minutes after contrast injection in the same image plane as the thermal images. DEMRI were also obtained along the LV short axis at several levels through the ablation lesion to assess the 3-D geometry of the lesion. DEMRI parameters were TI = 220 to 320ms [to “null” normal myocardium], flip angle=20 degrees, TE=1.7ms, TR=3.6ms, FOV=220cm, resolution 256x192, slice thickness=4mm, and averages=4.

Postmortem Examination
After the imaging protocol, the animals were injected with 20ml of a 20% solution of 2,3,5-triphenyltetrazolium chloride (TTC) and euthanized with an IV injection of high-molar potassium chloride solution. The hearts were excised and sectioned along the LV short axis through the ablation lesion center. Lesion location, morphology, and transmural extent were determined by gross examination and photographed for later comparison with the MR images.

**Thermography Image Generation**

To correct for shifting of the heart due to changes in diaphragm position 1-D registration was performed. Pre-heating and post-heating images were interpolated from an acquired resolution of 128x96 to a resolution of 512x384 to allow for sub-pixel registration. The post-heating image was shifted from -10 to +10 pixels along the direction of diaphragm motion and subtracted from the pre-heating image. The shifted image with the minimum absolute value difference from the initial pre-heating image was selected for further processing.

Because the catheter tip and heart/lung boundary can present an abrupt phase change in the image, variations of the tip position and heart shape related to heart rate variation and respiratory motion can lead to phase difference errors and subsequent temperature estimate errors. Also, imaging artifacts may be associated with arrhythmias and respiratory motion and lead to phase variations between images that are not related to
tissue heating. To approach the commonly intermittent nature of these sources of error, the “best” pre-heating image was selected by excluding the region around the catheter tip where heating was expected and choosing the pre-heating phase image with the minimum total phase difference from the post-heating phase image. A similar “multi-baseline” PRFST technique has been previously described.7

The phase difference image was then calculated between these pre and post-heating phase images and converted into a temperature difference map, as described by Equation 2, using standard methods.15 The baseline temperature obtained from the fiber-optic probe was then added to the temperature change map to produce a tissue temperature map.

Data Analysis

Thermography lesion extent was defined as the region with a temperature above 50°C corresponding to the irreversible tissue damage threshold of 50°C.6 DEMRI lesion extent was defined as the outer margin of the contrast enhanced lesion. Pathology lesion extent was defined as the outer margin of the hypo-pigmented region on photographs of the TTC stained tissue. This boundary has been observed to correspond to the outer margin of necrosis on histology.16 To normalize for differences in myocardial deformation between in-vivo diastolic imaging and ex-vivo pathology, lesion extent was reported as transmurality for LV short axis thermography images, DEMRI, and pathology.

Maximum lesion depth from the endocardium and the local LV wall thickness were measured using ImageJ software (Wayne Rasband, National Institutes of Health, USA).
Transmurality was defined as the maximum lesion depth divided by the local LV wall thickness.

The noise of the temperature change estimate was determined from the three pre-heating phase images. Phase difference images and corresponding temperature change maps were calculated between pairs of pre-heating images using the relationship described in Equation 2. Regions-of-interest were then defined at the catheter tip and mid LV anterior, lateral, posterior, inferior, and septal walls. Noise was calculated as $\sigma_{\Delta T_{\text{noise}}}$, the standard deviation of the temperature change within these un-heated regions of interest. $\sigma_{\Delta T_{\text{noise}}}$ is expected to reflect the noise during tissue heating to 50°C based on previous estimates of less than 0.5°C noise change with temperature changes exceeding 10°C.

Results:

Figures 2A to 2E illustrate the process of generating the tissue temperature image from pre-heating and post-heating phase images. The orange outer-lesion margin in figure 2E represents a tissue temperature greater than 50°C corresponding with the heating required for irreversible tissue damage. On this color scale, red would correspond to temperatures of 100°C and above.

The in-vitro relationship of the thermography temperature estimate to the fiber-optic probe temperature measurement is shown in Figure 3. A linear relationship was noted ($r^2 = 0.97$) with a tendency to underestimate temperature (50°C estimated at 50.0±3.1°C, P <0.05 and 90°C estimated at 86.3±4.3°C, P <0.05). The relationship improved when
considering thermography values up to 1.4mm from the fiber-optic probe tip location \( (r^2 = 0.99, 50\, ^\circ C \text{ estimated at } 50.1\pm 1.3\, ^\circ C, P <0.05 \text{ and } 90\, ^\circ C \text{ estimated at } 88.8\pm 1.8\, ^\circ C, P <0.05) \).

In all animals, an expanding thermal lesion was noted adjacent to the electrode as RF power was increased. (Figure 4) To assess if the post-heating change was related to a permanent change in tissue characteristics, tissue temperature maps were obtained during RF heating to an electrode temperature around 60°C and then 60 seconds after stopping RF power. Tissue temperatures greater than 50°C were noted during RF heating and were no longer visible by 60 seconds after stopping RF power in the four animals studied. (Figure 5)

The heating location by thermography (Figure 6A) corresponded to the lesion location on DEMRI (Figure 6B) and pathology (Figure 6C) in all animals. During prior studies we noted that thermography imaging planes parallel and perpendicular to the electrode axis did not reliably identify the maximum lesion extent. By reviewing the 3-D DEMRI lesion images, a LV short axis plane between the electrode tip and 4mm apical to the electrode tip appeared to regularly intersect the ablation lesion center for the electrode orientations used in this study. Using this imaging plane, the transmurality of the lesions determined by pathology, thermography, and DEMRI corresponded within 20%. (Figure 6D)
The mean temperature noise derived from the pre-heating phase images was 2.24°C +/- 1.08°C. (Figure 7A) The temperature change noise around the catheter tip was higher than for other regions (3.97°C +/-3.47°C vs. 1.90°C +/-0.43°C). However, spurious detection of temperature above 50°C was generally confined to the region adjacent to the catheter tip and did not extend deeper into the tissue as illustrated in Figure 7B. The resulting potential for non-normal noise distribution adjacent to the catheter tip should be considered when interpreting the temperature noise estimate in this region.

While 1-D registration and minimum phase difference pre-heating image selection were applied prior to phase image subtraction, these procedures were not always necessary. In this study, diaphragm motion was generally small and 93 out of 107 processed images did not require any registration. On the other hand, using pre-heating phase images other than the one immediately preceding post-heating imaging reduced spurious temperature readings in unheated portions of the myocardium in 35 out of 57 thermography images. This suggests that collecting multiple reference images prior to ablation may be useful for general application of this technique. Figure 8 illustrates cases where the use of 1-D registration and minimum phase difference selection reduced temperature noise in unheated regions of the heart.

Discussion

Successful arrhythmia ablation depends on permanently disrupting tissue conduction with the localized application of energy, most commonly RF energy. There is currently no
way of reliably assessing the extent of permanent tissue damage during cardiac RF ablation. In this study we found that myocardial temperature of 50°C as estimated by PRFST correlates well with ablation lesion location and extent on pathologic examination. Imaging during increasing power application demonstrated an increasing depth of myocardial heating and suggests that the technique may be useful for titrating power to desired lesion extent.

Comparison of PRFST to other techniques for assessing lesion extent

RF ablation lesions are formed by direct resistive heating of a narrow rim of tissue within 1mm from the electrode, and subsequent conduction of heat to the surrounding myocardium. The amount of resistive heating for a given amount of applied power depends on the efficiency of power transfer to the myocardium versus the blood pool. However, the efficiency of power transfer, and thus lesion size, can vary significantly with electrode tissue contact and surrounding blood flow.

X-ray fluoroscopy guided procedures are limited at assessing lesion extent because fluoroscopy does not directly visualize the electrode tissue contact interface and cannot visualize the soft tissue changes associated with lesion formation. The traditional variables monitored during RF energy application are electrode temperature, power, and impedance. However, these variables poorly characterize the efficiency of tissue power transfer and are also limited for predicting lesion extent. Saline irrigation reduces restrictions that local blood flow may impose on ablation power delivery but even further reduces the ability of electrode temperature to assess power transfer efficiency and
predict excessive tissue heating. This study suggests PRFST may be able to more directly assess myocardial ablation heating in-vivo. Tissue temperature assessment during saline irrigated catheter ablation was also demonstrated in-vitro. An MRI compatible irrigated catheter suitable for in-vivo use is under development.

Intra-cardiac echocardiography (ICE) has also been investigated for monitoring ablation lesion formation. ICE is able to directly visualize electrode-tissue contact and may detect tissue echogenicity changes after RF application. However, reliable ablation lesion visualization using ICE remains to be shown and restricted image plane orientation impairs the ability of ICE to characterize lesion extent and continuity between multiple ablation lesions. The ability to obtain arbitrary views of groups of ablation lesions is a potential strength of using MRI to guide cardiac ablation.

Comparison of PRFST to other MRI lesion visualization techniques

Though gadolinium-enhanced MRI provides good visualization of ablation lesions and can delineate gaps between ablation lesions, the need for repeated contrast injections limits its use for serial monitoring of ablation lesions during a procedure. The lesion border zone may also contain disrupted vasculature leading to delayed washout of gadolinium without reflecting permanent tissue damage. This may partially account for observations that DEMRI overestimates lesion size by an average of 1.4mm and that DEMRI performed 24 hours after ablation overestimates the enhancement seen 3 months after ablation. Non-contrast enhanced MRI of lesions using T2 weighted imaging has also been described. T2 weighted imaging is more suitable for serial lesion monitoring.
during an ablation procedure but is sensitive to tissue edema, which is common after RF ablation and can obscure lesion boundaries. By contrast, PRFST appears to visualize a graded temperature variation from the lesion periphery to center that may allow for different temperature thresholds to be associated with permanent and transient lesion characteristics.

Cardiac PRFST Temporal and Spatial Resolution

For true monitoring of lesion formation, the post-processing used in this study needs to be transitioned to real-time processing. This is not a fundamental limitation as acquiring, processing, and displaying up to two PRFST images per second has been demonstrated in other settings. However, the need to synchronize imaging to cardiac cycle motion places some additional constraints on cardiac PRFST performance.

In this feasibility study, a limited temporal resolution of 10 to 20 seconds was used. Though this restricted imaging to steady state heating conditions, a number of techniques are available to increase imaging speed. Echo planar imaging (EPI), collects multiple data samples for each MRI data acquisition period instead of the single data sample collected during GRE imaging. Parallel imaging schemes use multiple MRI receiver coils to compensate for undersampling of image data and have been combined with EPI to achieve PRFST rates of around 2 images per second. Alternatively, interleaved spiral gradient recalled echo imaging has been used to increase thermography image update rates to around 2 images per second. Extending such techniques to gated cardiac
thermography could permit temporal resolutions of less than 4 heartbeats and an ability to incorporate dynamic heating information into image updates every heart beat.

This study also used a relatively limited spatial resolution of 1.7x1.7x4mm. To assess the ability of a 4mm image slice thickness to produce a meaningful temperature map, the thermal equilibrium model described by Haines was used to determine the effect of averaging temperature across a 4mm slice at various distances from an ablation heating source. For a 100°C, 3mm diameter, spherical heating source the estimated error due to through slice averaging was 11%, 4%, and 2% at a distance of 0mm, 1mm, and 2mm from the electrode respectively. This suggests that thick slice imaging is capable of assessing the border extent of millimeter sized lesions, and that temperature may be estimated relatively close to the heating source if the peak heating is centered within the imaging plane. This is consistent with our observation that proper image plane selection was important for identifying maximum lesion extent in-vivo.

Though the PRFST technique described in this study is most directly applicable to ventricular arrhythmia ablation, the ability to monitor lesion formation during atrial ablation, for example during pulmonary vein isolation, would be attractive. Imaging the thin atrial wall requires smaller voxels than are typically used for cardiac MRI studies. DEMRI of left atrial ablation lesions has been performed using an acquired resolution around 1.25x1.25x2.5mm. Increasing the resolution used in this study to that level would increase the temperature estimate error by a factor of three which is likely unacceptable. Averaging can be used to increase the signal-to-noise ratio (SNR) but
requires longer imaging time. Local imaging coils, such as transesophageal or intra-vascular coils, may also be used to increase SNR while permitting more rapid imaging confined to the region of interest. Imaging with higher field MRI scanners is another consideration as phase SNR and the phase change for a given temperature change increase linearly with scanner field strength.\textsuperscript{12}

Cardiac PRFST Motion Sensitivity

Motion sensitivity is a limitation of PRFST.\textsuperscript{10, 25, 26} Because PRFST uses a difference measurement, changes in heart position and cardiac filling between pre-heating and post-heating imaging lead to temperature misestimation that could exceed the noise estimates provided in Figure 7. This effect is most significant when regions of rapid phase change become misaligned such as near the electrode and along heart/lung boundaries.\textsuperscript{17} To minimize these effects, several steps were taken. First, to reduce the extent of rapid phase variations around the catheter tip, a copper ablation electrode was used because its magnetic susceptibility is more closely matched to tissue as compared with stainless steel, platinum, or gold. Imaging parameters were also adjusted to reduce cardiac motion during data acquisition periods including restricting imaging to a 90ms diastolic window and using a shorter TE, 9ms, than is typically used for PRFST applications. Small shifts in heart position between images were also corrected by 1-D registration along the direction of diaphragm motion. In-addition, the minimum phase error reference image was used for the temperature difference measurement to help correct for changes in heart geometry or motion artifacts that were not corrected using the previous techniques.
Finally, pre-heating reference images were obtained within 5 minutes of RF heating images to reduce the impact of phase drift due to thermal variations in the MR scanner field shim coils. Using these adjustments, PRFST was able to acceptably detect the thermal threshold of myocardial destruction and PRFST detected heating appeared to be reversible after tissue cooling.

Further investigation is required to determine how much physiologic variation is tolerable for reliable cardiac lesion imaging. Physiologic parameters were closely regulated for this feasibility study. Heart rate was carefully controlled within 10 bpm between pre-heating and post-heating images and repeat pre-heating images were obtained if a cardiac filling variation due to fluid administration or heart rate change was observed. The best images were obtained when no respiratory motion was observed during breath holding. These limitations must be relaxed for practical application.

Respiratory gating has been used to permit PRFST in free breathing subjects. Referenceless PRFST is another technique that can reduce motion sensitivity by eliminating the need to collect a preheating image. This method estimates the preheating phase by extrapolating from unheated regions of the image. Reducing the motion sensitivity of PRFST is an area of active investigation.

Additional PRFST Accuracy Considerations

The temperature noise estimates in this study were meant to serve as a baseline achieved under controlled conditions. There are a number of sources of uncertainty in PRFST, in
addition to those discussed above, which could contribute to higher temperature estimate errors in practice. These factors include imaging system noise\textsuperscript{15}, uncertainty in the baseline temperature, uncertainty in the calibration of the PRF shift in-vivo\textsuperscript{12}, and drift of the static magnetic field over time\textsuperscript{27}. In addition, temperature induced changes in tissue magnetic susceptibility alter the temperature dependence of the PRF and can be affected by the orientation of the heating source\textsuperscript{29, 30}. Techniques to mitigate these sources of error have been proposed\textsuperscript{27, 29}. Even with these uncertainties a number of animal studies have demonstrated good correlation between PRFST assessed tissue heating and the extent of the resulting ablated region\textsuperscript{12}. Growing clinical experience with PRFST is encouraging but supports the need for improved motion artifact mitigation techniques\textsuperscript{12, 31}.

\textbf{Conclusion:}

This study demonstrated the feasibility of non-invasive detection of tissue heating during cardiac RF ablation using PRFST thermography. To our knowledge this represents the first directed imaging of maximum ablation lesion extent during cardiac RF application. Larger studies implementing free-breathing imaging, real-time image display, and clinically relevant ablation protocols are needed to assess the practical utility and accuracy of cardiac PRFST. Still, PRFST appears to be a promising technique for monitoring lesion formation and may allow for more accurate placement and titration of ablation, possibly reducing arrhythmia recurrences.

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\textbf{Conflict of Interest Disclosures:} Drs Halperin, Berger, and Lardo serve as scientific advisors for Boston Scientific Inc. Drs Halperin and Berger hold a patent on MRI-compatible catheter technology. The Johns Hopkins University Advisory Committee on Conflict of Interest manages all commercial arrangements.
References:


Figure Legends:

Figure 1. Gradient Recalled Echo MR images. A) Image acquired with a TE= T2⁎ muscle =40ms. Note the image blurring due to cardiac motion over the longer imaging period. B) Image acquired with a TE=9ms. Note the significant improvement in image clarity with the shorter TE.

Figure 2. Data processing for cardiac RF ablation PRFS thermography. The registered pre-heating phase image (B) is subtracted from the post-heating phase image (A) to give a phase difference image (C). Low signal intensity areas of the anatomic image are masked off from further processing. Phase unwrapping (not shown) is performed on the phase difference image (C) prior to conversion to a temperature change image (D) using Equation 2. The baseline temperature obtained from the fiber-optic temperature probe is then added to obtain the tissue temperature image. E) Illustrates the tissue temperature image overlaid on the anatomic image for reference. The orange lesion border indicates 50°C, chosen to correspond to irreversible tissue damage.
Figure 3. In-vitro correlation of thermography to fiber-optic temperature probe measurement within (A) 0.5 acquired pixels (0.85mm) and (B) 1.6 acquired pixels (1.4mm) of the fiber-optic probe tip.

Figure 4. In-vivo thermal lesion expansion with increasing RF power was noted in all animals. The blue circle highlights ablation electrode position.

Figure 5. The thermal lesion was not visible 60 seconds after stopping RF power in all animals studied. A) 50°C thermal lesion during 10 Watts of RF power application and (B) 60 seconds after stopping RF power. The blue circle highlights ablation electrode position.

Figure 6. Comparison of thermography heating location and extent (A) to delayed gadolinium enhancement MRI (B) and pathology (C). The heating location and maximum depth by thermography corresponded well to the lesion location and depth on DEMRI and pathology in all animals. D) Lesion transmurality by thermography was within 20% of that measured by pathology and delayed gadolinium-enhanced MRI. Each color represents one animal.

Figure 7. Temperature noise derived from pre-heating phase images for different regions of the left ventricle (A). The increased noise around the catheter tip was largely confined to the region immediately around the tip position as shown in (B). Temperature noise can increase beyond these values with larger shifts in catheter tip location, increasing time...
between the pre-heating and post-heating image collection, and misalignment of the heart due to changes in heart rate and diaphragm position.

**Figure 8.** A) Example of temperature estimate error caused by a shift in the diaphragm position between pre-heating and post-heating images. B) Reduction of temperature estimate error by shifting images to realign the heart on pre and post-heating images. C) Thermography image generated using the pre-heating image immediately preceding the post-heating image. Errors result when heart motion or image artifact lead to phase changes that are not corrected by simple image registration. D) Reduction of noise by selection of the “minimum phase difference” pre-heating image.
A) TE=40ms

B) TE=9ms
A) Post-heating Phase during 24W

B) Pre-heating Phase Image

C) Phase Difference $\Delta \phi$

$$\Delta T = (-27.69^\circ C/\text{rad}) \Delta \phi$$

D) Temperature Change

Pre-heating Temperature (fiber optic)

E) Tissue temperature overlaid on anatomic image

The orange lesion border indicates 50°C and Red indicates 100°C
A) Thermography vs Fiberoptic Temperature (0.5 pixel radius)

\[(4.7 \pm 1.7) + (0.91 \pm 0.029) \times [95\% \text{ CI}]\]

\[R^2 = 0.977\]

B) Thermography vs Fiberoptic Temperature (1.6 pixel radius)

\[(1.6 \pm 0.72) + (0.97 \pm 0.012) \times [95\% \text{ CI}]\]

\[R^2 = 0.996\]
A) During 10 Watts RF power

B) 60 seconds after stopping 10W
B) Delayed Gadolinium Enhancement image

D) Lesion Transmurality by Pathology and MRI

A) Temperature Change > 50°C

C) TTC Stained Gross Pathology
A) Pre-heating Temperature Noise by Heart Region

B) Pre-heating Temperature Noise > 50°C
A) Without image registration

B) With image registration

C) Using default pre-heating image

D) Using minimum phase difference pre-heating image
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Figure Legends:

**Figure 1s**: Effect of slice thickness on temperature estimate error based on the thermal equilibrium model proposed by Haines (19). Model parameters are: electrode diameter 3mm, electrode temperature 100°C, ambient temperature 37°C. A) Plot of temperature as a function of x and y position on the z = 0 plane through the center of a 100°C, 3mm diameter, spherical electrode. B) Temperature profiles in the through slice direction for a 4mm slice centered on the electrode position at different distances from the electrode. Note that the through slice temperature variation decreases with increasing distance from the electrode. C) Exact temperature (at z=0) versus temperature averaged over 4mm slice (z=-2 to +2mm) at different distances from center of electrode. D) Percentage error of temperature averaged over 4mm slice versus exact temperature (at z=0) at various distances from the electrode. Note that the error due to through slice averaging decreases with increasing distance from the electrode.

Figures:

**Figure 1s:**

A) Temperature vs. x and y distance from 100°C, 3mm diameter electrode
B) Temperature across 4mm thick slice at various distances from 100°C electrode surface
C) Temperature estimate at various distances from 100°C electrode surface
D) Temperature error for 4mm slice at various distances from 100°C electrode surface