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Real time assessment of RF cardiac tissue ablation with optical spectroscopy

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Abstract: An optical spectroscopy approach is demonstrated allowing for critical parameters during RF ablation of cardiac tissue to be evaluated in real time. The method is based on incorporating in a typical ablation catheter transmitting and receiving fibers that terminate at the tip of the catheter. By analyzing the spectral characteristics of the NIR diffusely reflected light, information is obtained on such parameters as, catheter-tissue proximity, lesion formation, depth of penetration of the lesion, formation of char during the ablation, formation of coagulum around the ablation site, differentiation of ablated from healthy tissue, and recognition of micro-bubble formation in the tissue

OCIS codes: (170.6510) Spectroscopy, tissue diagnostics; (170.3890) Medical optics instrumentation.

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1. Introduction

The most frequent cause of cardiac arrhythmias is an abnormal routing of electrical signals generated in the endocardial tissue. Catheter ablation can be used to treat cases when arrhythmia cannot be controlled with medication, or in patients that cannot tolerate these medications. Using an ablation catheter or similar probe having an energy-emitting element, usually in the form of Radiofrequency (RF) energy [1-3], a sufficient amount of energy in the location of suspected centers of this electrical misfiring near the atrial or ventricular walls is delivered leading to the formation of a lesion. These lesions are intended to stop the irregular beating of the heart by creating non-conductive barriers between regions of abnormal electrical activity [4]. Successful treatment depends on the location of the ablation within the heart as well as the spatial characteristics of the lesion.

Since contact of the catheter with the tissue is critical for the formation of the lesion, various methods have been proposed to address this issue during surgery including monitoring of the electrical impedance between the catheter electrode and the dispersive electrode (which utilizes the difference in resistivity between blood and endocardium) and the temperature at the tip of the catheter [5-7]. However, in current practice these methods do not provide a reliable tool to determine proper contact of the catheter with the tissue. As a

result, experience and skill of the electrophysiologist performing the procedure play a major part on the clinical outcome. The effectiveness of lesion therapy is evaluated by a post ablation monitoring of the electrical signals produced in the heart. If it is determined that signals responsible for arrhythmia are still present (suggesting that the lesion was not adequately formed), additional lesions can be created to form a line of lesions to block passage of abnormal currents. However, there is currently no method to assess in real time how he lesion is formed. The ablation process can also cause undesirable side-effects such as charring of the tissue, localized blood coagulation, and vaporization of tissue water that can lead to steam pocket formation and subsequent implosion (steam pop) that can cause severe complications [8,9]. All these side effects can be mitigated by adjusting the RF power of the catheter if the operator was aware of their development [10,11]. Clearly, limited to post ablation evaluation is undesirable since correction requires additional medical procedures while the surgeon has minimal knowledge regarding the development of undesirable ablation side effects. Thus, there is a need for the development of a guidance tool that could help evaluate the lesion in real time as it is being formed in the tissue.

Thermal coagulation of myocardium leads to significant changes in its optical properties [12-16]. For the case of myocardium coagulation via RF ablation, Swartling et al reported that the changes in the optical properties in the near infrared (NIR) spectral region include an increase of the scattering coefficient (≈ 5% higher), a smaller decrease in the scattering anisotropy factor (≈ 2% lower) and an increase in the absorption coefficient (≈ 20% higher) [17]. We hypothesized that these changes in the optical properties of the RF ablated cardiac tissue can be used to provide in vivo monitoring of lesion formation parameters. Furthermore, considering that absorption by blood and myocardium in the NIR spectral region is minimal, we hypothesized that such in vivo monitoring method may be based on NIR light scattering spectroscopy and could be employed through the vascular system, preferably as a fiber-optic attachment to the RF ablation catheter.

In this work, we demonstrate a method for the evaluation of lesion formation via RF ablation in real-time using near infrared (NIR) light scattering spectroscopy. To execute this work, the ablation catheter is modified to incorporate spatially separated light emitting and receiving fibers that are in contact with the as formed lesion at the tip of the catheter. Spectral analysis of the light collected by the receiving fiber allows detection of key parameters such as, contact of the catheter with the tissue, onset of lesion formation, depth of penetration of the lesion, formation of char or coagulum during the ablation.

2. Experimental Method

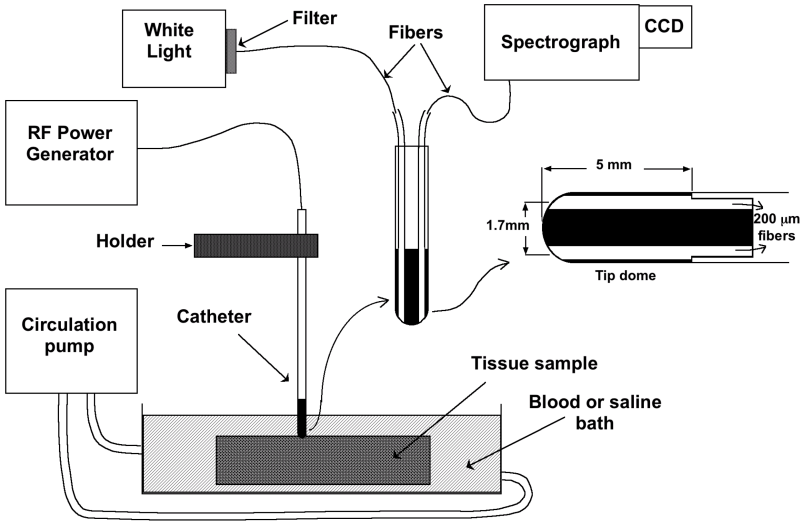

Fig. 1. Schematic depicting the experimental setup. The tip of the RF ablation catheter incorporates two fibers to enable acquisition of spectra from the location of lesion formation.

The experimental arrangement is depicted in Fig. 1. Fresh bovine hearts obtained from a meat processing facility were used to procure samples with approximate dimensions of 10 cm X 5 cm X 2 cm. The samples were positioned in a holder at the bottom a container filled with either saline solution or heparinized bovine blood. A circulation and heating system was used to sustain a flow around the sample as well as control the temperature to 36 degrees Celsius. The RF ablation catheter was positioned vertically in the surface of the sample and kept at the fixed location during each ablation via a specially designed holder. This holder also enabled the application of a constant contact force of the catheter on the tissue surface at 10 g chosen to simulate typical conditions during in vivo applications.

A schematic diagram of the catheter is also shown in Fig. 1. The catheter was custom made and involved an open irrigation design [11]. However, no irrigation was used during our experiments to allow for a monotonic temperature gradient with tissue thickness at the location of lesion formation (open irrigation causes cooling of the surface and temperatures below the surface can be higher). This catheter contained two fibers, 200 μm in diameter. The fibers were terminating at diametrically opposite sites at the distal end of the catheter with their tips aligned with the catheter's outer metallic surface. The lateral separation between the fibers was 1.7 mm as depicted in Fig. 1. One fiber was connected to a white light source after passing through a 600 nm long wavelength pass filter and was used to deliver the illumination to the tissue. The other fiber was used to collect the scattered light and it was coupled to a spectrograph to analyze and record the spectrum of the scattered light from the tissue. In this way, a sequence of spectra was acquired at a rate of one spectrum per second. The tissue was ablated for periods of time between 30 sec and 90 seconds using variable settings in the RF power generator to create lesion of various depths and formation depth rates. After the experiment, the tissue was dissected in order to determine via visual inspection and measurement the final depth of the lesion.

3. Experimental Results

Figure 2 shows a sequence of spectra obtained prior to, during and after ablation that resulted

in a lesion that was 2 mm in depth. The onset and termination of RF power delivery are denoted with “START” and “STOP”, respectively. These spectra represent raw data and have not been normalized for instrument response. The spectra allow to directly appreciate the changes in intensity and spectral characteristics of the scattered light as collected by the receiving fiber occurring during tissue ablation. With the termination of the ablation, there is no additional change observed in the spectrum indicating that the changes in the spectral profile are permanent.

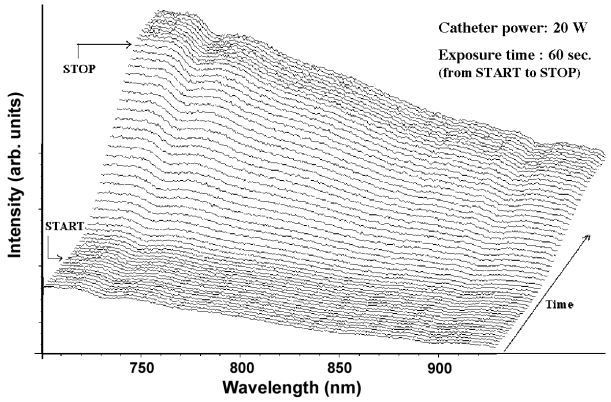

Fig. 2. Raw spectra obtained prior to, during and, after RF ablation highlight the changes in the light scattering spectrum resulting from tissue modification.

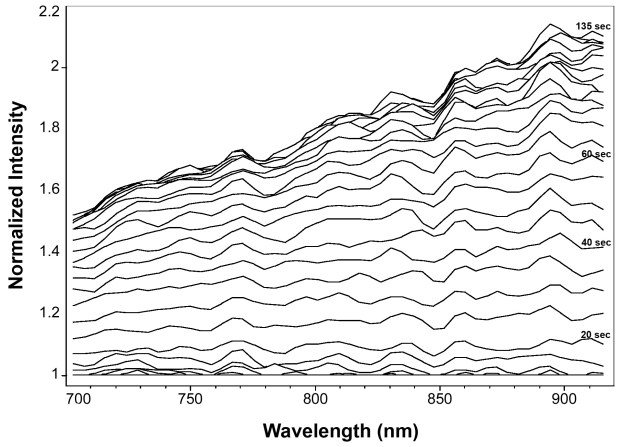

Fig. 3. Normalized (to t=0) spectra at different times during RF ablation of cardiac tissue

To better quantify these changes, the as recorded spectra were normalized (divided) to the spectrum recorded just before the RF power was turned on. Thus, at the onset of ablation the normalized intensity is about 1 (within the noise of the measurement) through the entire spectral range. A typical example of the evolution of the spectral profile after normalization during RF ablation that resulted in a lesion that was 5 mm deep is shown in Fig. 3. For clarity, spectral profiles recorded every 5 seconds from the onset of ablation are shown and the corresponding time at which some of these spectral profiles were collected is provided on the right hand side. There are two characteristic changes in the evolution of the spectral

profile of the detected scattered light during lesion formation: a) The intensity of the signal increases with time duration of RF energy deposition and lesion formation; b) The ralative increase in signal intensity is larger for longer wavelengths leading to a change in the slope of the spectral profile from its original horizontal direction towards 45 degrees.

The results shown in Fig. 3 were consistently reproduced in every site tested in tissues obtained from multiple bovine hearts. The increase of the signal intensity after the RF power was turned on provided a clear indication in real time that a lesion started forming. Since both, the intensity and the slope of the normalized spectral profile change with time duration of ablation and thus, the depth of the lesion, we explored if a direct correlation can be found that can be used to develop a method to assess lesion depth in real time. A preliminary analysis of the results suggested that there is a tissue dependant variability in the measured absolute value of the intensity. In addition, in a clinical environment, motion of the heart and unstable contact of the catheter with the surface of the tissue could make a measurement of the absolute intensity very challenging. On the other hand, the slope of the normalized spectral profile is independent of the absolute intensity of the signal and possibly, a more reliable optical signature of the lesion formation parameters.

To test this concept, we calculated the ratio of the spectral intensity at 910 nm over that at 710 nm. This quantity is referred to in the rest of this document as “slope”. We then plotted the value of the slope as a function of the final lesion depth using data obtained from lesions created using different ablation times and power settings resulting on wide range of lesion depths. Experiments were performed with the tissue sample inside a blood bath and in saline solution. The results were quantitatively and qualitatively identical indicating that the blood does affect the measurements. Figure 4 summarizes our experimental results showing the depth of the ablated tissue and the corresponding slope of the accompanying spectral profile. These results indicate an almost linear relationship between these two parameters for lesion

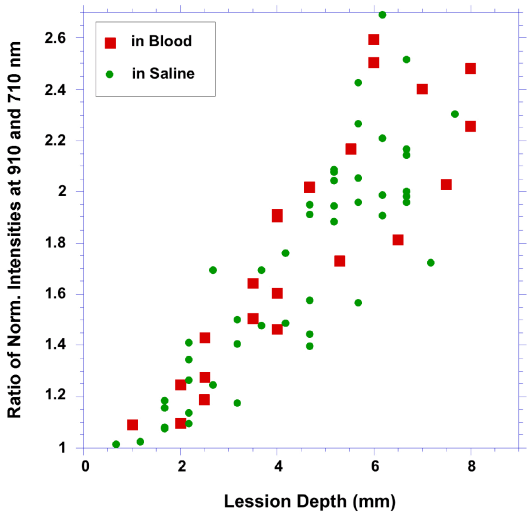

Fig. 4. The dependence of the slope of the normalized spectra on the depth of the ablated tissue for experiments performed in saline solution (circles) and heparinized blood (squares).

depths up to about 6 mm. Above 6 mm depth, the experimental error increases significantly in part for reasons that will be discussed later.

Additional information can be obtained when the slope of the spectrum is monitored during

ablation. Figure 5 shows the slope vs. time for 5 different ablations that resulted to lesions with depths of about 1 mm, 2 mm, 4 mm, 6 mm and 8 mm. It is appreciated in this figure the different rates by which the slope is changing depending on the power settings of the catheter. In addition, within each time profile of the spectral ratio slope during ablation, the change in the value of the ratio is smooth suggesting that the larger spread in the results around a mean value for each depth shown in Fig. 4 is due to tissue variability and not to experimental error arising form the instrumentation. From this type of data, one can extract the rate of tissue ablation since the slope is related to the depth of the lesion as shown in figure 4. This can be particular important for deeper lesions where direct measurement of the depth using the fibers

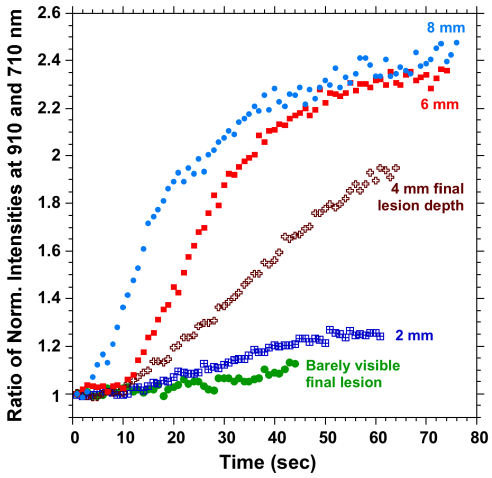

Fig. 5. Profiles of the slope of the normalized spectrum as a function of time during 5 different ablations that resulted to lesions with depths of 1 mm, 2mm, 4mm, 6mm and 8 mm.

may be impossible. More specifically, the measurement of the slope can provide relatively accurate results for lesion of up to 6 mm (in the bovine tissue used in this experiment) as demonstrated in Fig. 4. However, by measuring the rate of tissue ablation during the initial 6 mm, one can extrapolate the ablation time needed to create lesions of larger depth

During execution of the experiments and for higher power setting of the RF generator and/or longer ablation times, we frequently observed the formation of tissue charring or blood coagulum [11] as was revealed by the post-ablation examination of the tissue sample. These undesirable during surgery side effects of the ablation process consistently resulted in a change in the detected light scattering spectral profile. Figure 6 shows typical examples of the normalized spectra in the presence of coagulum and charring formed during ablations that resulted to about 7 mm deep lesions. The spectrum obtained in the presence of coagulum shows the presence of two valleys located at about 775 nm and 865 nm. This indicates the presence of two absorption peaks at these spectral locations arising from the optical properties of the coagulum. The spectrum in the presence of charring is similar to that of coagulum but it contains only the first absorption peak at 775 nm. However, it is evident by the lower values of the normalized ratio at the shorter wavelengths (typically between 0.8 and 1.1 at ≈ 700 nm instead of over 1.4 as suggested by the evolution of the spectral profile shown in Fig. 3), there is an underlying broader absorption spectral band at shorter wavelengths in the spectral region covered in Fig. 6 for both, tissue charring and coagulum. These characteristic spectral features indicate the feasibility to provide in real time information to the operator to detect the onset of tissue charring or formation of blood

coagulum during ablation so that appropriate action can be taken to stop further development.

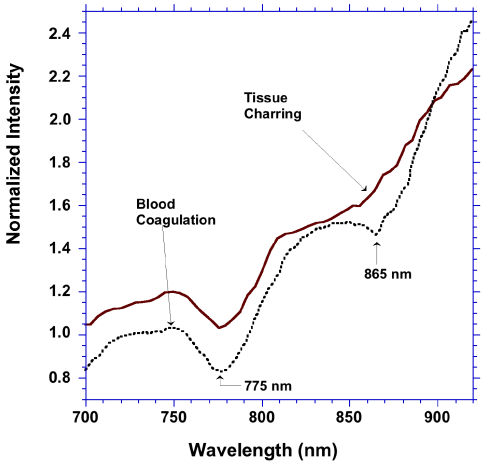

Fig. 6. Normalized light scattering spectrum in the presence of blood coagulum and tissue charring from RF ablation of normal bovine cardiac tissue.

4. Discussion

The ex-vivo experimental results discussed in this work suggest that NIR light scattering spectroscopy implemented via optical fibers positioned at the tip of the RF ablation catheter provide in real time information that is directly related to the lesion formation parameters. We will next discuss in more details these parameters and how they can address current unmet needs in a clinical setting.

a) Establishing contact of catheter with the tissue

The detected signal intensity when the catheter is inside blood but not in contact with tissue increases by approximately a factor of 2 when contact is established. This observation is very repeatable and can be used as a reliable complementary guidance tool during navigation of the catheter through the heart's compartments to the target location. Currently, the operator uses rotational movements and pressure to ensure proper contact of the tip of the catheter with the tissue.

b) Finding location of pre-existing lesion

The difference in signal intensity when the catheter is in contact with normal tissue compared to that when in contact with an ablation lesion can be as high as a factor of 2 or larger as demonstrated in Fig. 3. Furthermore, the slope of the spectral profile as defined in the previous section changes significantly (see Figs. 4 and 5) providing an additional method to accurately detect contact with a preexisting lesion if a follow up ablation is needed in the same location. It is also possible to use the spectral information to detect contact with abnormal tissue. Specifically, comparison of the as detected spectrum to that of healthy and ablated tissue may yield information to identify locations of tissue alteration (such as calcification) due to pre-existing health conditions. Such conditions may lead to cardiac arrhythmia and thus, detecting the abnormal tissue regions can assist to guide the catheter to the location that needs to be ablated. Although this novel aspect has not been explored in the current study, the potential of this method to execute such a tasks is apparent if the pre-existing condition causes alteration of the optical properties in the NIR of the affected tissue

region.

c) Detection of onset of ablation

The results shown in Figs 2 through 5 demonstrate that the onset of ablation is accompanied by a sharp rise in the detected signal intensity as well as a change in the slope. In a clinical setting, this can provide direct information that the energy is delivered properly on the target location and the lesion is forming. Currently, feedback to the physician is provided by the shift in impedance and increase in temperature [18]. These parameters are readily available to the operator in current high-end instrumentation but provide indirect information since, for example, the temperature of the tip (or impedance) can increase upon RF energy delivery without proper contact of the catheter with the tissue.

d) Assessment of lesion depth

As discussed earlier, there is currently no method to assess the depth of the lesion. The results shown in Figs. 4 demonstrate that using a spectral ratio method such as that adopted in this work (defined here as the "slope" of the spectral profile) leads to a parameter that monotonically changes with the depth of the RF ablation lesion. We postulate that this can be used to develop a calibration method that will enable an estimation of the spatial characteristics of the lesion in real time. The mechanism that leads to the relationship of the spectral characteristics of the detected scattered light to lesion depth may be complex. The change in the optical properties of the ablated tissue as described in refs. 12-17 is a major part of this mechanism and best explains the increase in the scattering intensity with the formation of the lesion. In addition, the dependence of the scattering coefficient of the normal and ablated tissue on the wavelength of the light can introduce spectral changes that depend on the tissue or lesion depth that can be revealed by a spectral ratio technique as discussed in references 19 and 20. Due to the complexity of this issue, we will limit the discussion in this report to only the presentation of our experimental findings.

e) Assessment of rate of lesion formation

If the method to translate the spectral information in to lesion depths is validated, it will enable monitoring in real time the rate by which the lesions depth increases as demonstrated in Fig. 5. This information may be valuable in various ways. For example, as discussed in the previous section, this method is sensitive to ablation lesion depths up to approximately 6 mm for the tissue model used in this work. If a lesion with final depth larger than that is required, monitoring the rate by which the lesion is created at the early stages can help project the time needed to continue the ablation in order to achieve the desired final depth. In addition, a high rate for lesion formation may be a precursor to delivering energy at a higher rate than that required to avoid overheating of the tissue that can lead to steam pop formation (an issue that is discussed in more detail later).

f) Detection of tissue charring and blood coagulation

Tissue charring and thrombus of blood coagulation are undesirable side-effect during RF ablation procedures. These changes take place in the area adjacent to the catheter and as a result, they can strongly affect the spectral characteristics of the detected signal. The characteristic changes of the normalized spectral profiles shown in Fig. 6 demonstrate that this method offer a way to detect the presence of tissue charring or blood coagulation. Preliminary experiments showed that thrombus can be detected even if small quantities were found during the post-examination of the ablated area. Similarly, the detection of charring was possible even when a very small amount was visible by naked eye in the location of lesion formation during post-examination. The most profound change in the spectral characteristics due to the formation of charring or blood coagulation is the reduction of the signal intensity at shorter wavelengths leading to a lower value of the normalized intensity in

the 700 nm- 800 nm spectral range. During our experiments, this signal decline was clearly observable at later times of ablation with higher RF power settings following a "normal" increase in the signal (such as that shown in Fig. 2) in the early part. The origin of this change in the spectral profile is likely a broad absorption band resulting from coagulation of hemoglobin (and corresponding changes in myoglobin) [21]. The narrower in spectral range absorption bands centered at 775 nm and 865 nm as observed in Fig. 6 may be secondary specific features of this broader absorption band associated with coagulation of hemoglobin (both bands) and myoglobin (the 775 nm only)

The reduction in signal intensity at shorter wavelengths due to this absorption band affects the evaluation of the lesion depth as performed in this work through the utilization of the slope of the normalized spectrum. Therefore, it is imperative that a correction factor must be devised to account for the change in the slope for the evaluation of lesion depth in the presence of spectral characteristics from charring on coagulation. It must be emphasized that in clinical practice the tissue temperature is typically monitored to avoid coagulation affects. It is therefore expected that this issue will represent a small fraction of the procedures and when it occurs, this method provide the means to be recognized early and mitigated via changes in the RF generator power settings. In current clinical practice, there is no information available to the operator regarding the development of these important side effects which can be undetected until there are symptomatic evidence.

g) Detection of precursors to steam-pop formation

One of the most dangerous side effects of RF ablation is explosive release of gas resulting from excessive heating of the tissue, also referred to as steam pop formation. It is believed that an early sign of tissue overheating that can lead to an explosive release of gas is formation of "microbubbles" [22-24]. The onset of microbubble formation can be as early as about 1 minute prior to explosive release [23] thus, the development of this process is slow. Such microbubbles will induce large changes in the index of refraction within the tissue thus greatly enhancing the scattering of light traveling from the illumination fiber towards the receiving fiber. In turn, this will yield a decrease in the signal intensity through the entire spectral range of detection. Due to the slow development of this process and its probabilistic nature [25], an extensive study is required to validate this hypothesis under relevant conditions which is outside the focus of this report. However, our limited preliminary results are in agreement supporting the potential of this method to also address this important issue.

Ultrasound and magnetic resonance techniques are currently under investigation for the evaluation in real time of lesion formation parameters during RF ablation [26, 27]. Arguably, the optical spectroscopy method described in this work offers a most attractive approach providing monitoring of multiple parameters of lesion formation with minimally expensive instrumentation that is compatible with existing catheter designs.

To transfer this technology in a clinical setting, various modifications are needed for two main reasons. First, the target location is in a moving organ. Second, the catheter is not always positioned vertically with respect to the surface of the tissue. To address the first issue, signal registration issues need to be addressed via synchronization and phase-locking of signal collection to cardiac movement during the procedure. Signal collection must be performed at time intervals much shorter than the cardiac movement cycle. Under such conditions, laser illumination at appropriate discrete wavelengths may be used to replace the white light source used in this work in order to achieve adequate signal-to-noise ratio. To address the second major issue, one or more fibers may be added on the side of the catheter in order to probe the tissue in the case where the catheter is at an angle different than normal to the tissue's surface. A more advanced system could involve a scheme in which a set of fibers terminating at different locations at the tip of the catheter can be used alternately for

illumination or collection of scattered light in a specific sequence that will allow for more accurate assessment of the characteristic of ablation and the surrounding the catheter environment. Overall, transferring this technology to the clinic may be a challenging but a solvable problem.

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