ABSTRACT. Catheter ablation for atrial fibrillation has become a first line treatment for selected paroxysmal atrial fibrillation patients. However, clinical results are not satisfying, with recurrence rates at 1-year follow-up exceeding around 60% in broader registries. A widely accepted cause of recurrence after initially successful therapy is pulmonary vein reconnection because of non-transmural necrosis or lack of continuity in ablation lines. There is great interest in developing new tools to assist the electrophysiologist with direct information on lesion formation, including depth and lateral extension, in the tissue surrounding the ablation electrode. We introduce an integrated catheter design with capabilities for simultaneous radiofrequency ablation and imaging based on polarization-sensitive optical coherence reflectometry. The feasibility of in vivo applications is demonstrated. This technology allows analysis of how tissue optical properties change during the ablation as a consequence of protein denaturation in the extracellular matrix of muscular fibers upon heating. The distance and contact quality between catheter tip and tissue have also been evaluated with this technique. This integrated catheter design opens a new path to better clinical outcomes by providing direct real-time information on the efficacy of ablation and the local environment of the electrode, thus increasing the chances of successful therapies.

KEYWORDS. atrial fibrillation, image guidance, polarization-sensitive optical coherence tomography, radiofrequency catheter ablation.

Introduction

Circumferential pulmonary vein isolation (PVI) based on radiofrequency ablation (RFA) is becoming a minimally invasive standard of care for atrial fibrillation. Yet, clinical results remain hampered by the high rate of recurrences.1 Several reports have highlighted the key role of suboptimal ablation, including non-transmural necrosis and lack of continuity in linear lesions, as a mechanism of recurrence after initially successful sinus rhythm restoration.2–4 The dispersion of results is affected by the strong variability of biophysical parameters with influence in the desired tissue-heating effect, including changes in the density and orientation of muscular fibers in myocardial tissue between patients. Contact quality between electrode and atrial wall, as well as local blood flow, are factors known to affect lesion formation significantly. Thus, the electrical power...
applied or treatment times do not generally correlate with lesion size. Consequently, radiofrequency (RF) application must be tailored at each spot to prevent overheating damage and increase risk of cardiac perforation, or missing the required transmurality, which may lead to pulmonary vein reconnection.

Recent research in therapeutic catheter technology is trying to address this problem through real-time monitoring of RFA using cross-sectional imaging technologies, such as ultrasound (US) or optical coherence tomography (OCT). OCT may draw some advantage from its higher axial resolution (≈10 μm). This accuracy is crucial for example in the thin wall of the atrium, where the 200 μm typical of US may correspond to more than 20% of the total thickness in thinner walls. Previous work has evaluated the feasibility of cardiac ablation monitoring with OCT, but structural images do not always show clear differences. However, differentiation between ablated and healthy tissue has been demonstrated by polarization sensitive OCT (PS-OCT) imaging, supported by loss of the birefringence during the thermal denaturation of collagen.

Until now, complex systems have been designed for in vivo RFA real-time monitoring. Reported solutions involve two catheters attached to each other, and have several disadvantages: 1) implementation complexity of mechanical beam scanners combined with an electrode-based ablation device; 2) the observed tissue is only adjacent to a region of RF treatment, with a limited field of view; 3) risk of losing the required alignment between therapeutic catheter and the guidance system during the procedure. These complications in the device design limit application of these approaches in the short-term treatment of real patients.

An integrated catheter enabling simultaneous RFA and polarization-sensitive optical coherence reflectometry (PS-OCR) has been reported for the first time. On the basis of this design, assessment of catheter contact, differentiation between ablated and healthy tissue, and the first in vivo procedure with an integrated RF catheter providing real-time optical tissue evaluation is demonstrated. For this procedure, percutaneous ablation guided by PS-OCR was performed through both the transfemoral and the transapical approach in a pig model.

Methods

Freshly excised right ventricular wedges from swine hearts were used for in vitro characterization of contact feedback and differentiation of healthy and previously ablated tissue with PS-OCR imaging. Following the onset of general anesthesia, a thoracotomy was performed, and the heart was rapidly excised and placed in a blood bath. In this case, the in vitro model has been chosen for suitable visual control over the catheter position. The RF catheter was guided by a single-mode optical fiber followed by an off-the-shelf gradient index rod lens (GRINTech GmbH, Jena, Germany), which is implemented in a customized 7F steerable RFA catheter (Vascomed GmbH, Binzen, Germany), without modifying its mechanical properties; as a consequence, handling is identical to a clinical ablation catheter. More structural details are shown in Figure 1a. The PS-OCR system is based on OCS1300SS (Thorlabs Inc., Sterling, VA) with a frequency swept laser centered at 1300 nm. Light from the laser source is temporally multiplexed between two orthogonal polarization states, and the interference fringe signals are detected using a polarization sensitive balanced photo-detector to measure the phase retardation (PR) between polarization states of light induced by the biological tissue birefringence properties.

An in vivo protocol was selected to verify the feasibility of this technique in real therapies. The study protocol was approved by the ethics committee of the Foundation for Biomedical Research of La Paz University Hospital. The pig (Large-white, 35 kg) was anesthetized by intramuscular injection of ketamine (12 mg/kg) and midazolam (0.5 mg/kg), and intubated and mechanically ventilated. Arterial pressure and electrocardiogram were monitored. During the procedure, sedation was maintained with propofol (11 mg/kg/h) and fentanyl (6 μg/kg/h) infusion and inhaled anesthesia with 2–3% isoflurane. Bilateral femoral venous percutaneous puncture was performed and 8F introducers were placed as shown in Figure 1b. The experimental ablation catheter was advanced through the right femoral vein under fluoroscopy, reaching the right cardiac chambers. A long sheath was advanced via the left femoral vein for dye injection to guide the catheter and determine the intracardiac position. The left femoral artery was also percutaneously punctured and a 6F sheath was inserted to guide a 5F pigtail catheter to the ascending aorta, for anatomic reference and to monitor arterial pressure. Unfractionated heparin (100 UI/kg), lidocaine (80 mg), and amiodarone (150 mg) were intravenously administered before the beginning of the procedure.

To access the left cardiac chambers, we used a novel approach as an alternative to the transseptal procedure: a direct closed-chest percutaneous puncture of the left ventricular (Figure 1c). In the subxyphoid space, the point of access of the needle was located by fluoroscopy and palpation of the apical beat. The apex was punctured and an 8F introducer was placed using the Seldinger technique. This technique has been previously described and was verified in two pigs with ultrasonographic control, showing absence of severe pericardial bleeding or cardiac tamponade. This approach significantly simplifies the access to the left chambers, allowing fast entry into the cavities and direct control of the catheter, avoiding the technically demanding transseptal puncture and its potential related complications.

As in the in vitro protocol, the optical signal during RFA was measured using an experimental set-up previously described. The eight in vivo applications were carried out under the Atakr II (Medtronic Inc., St. Paul, MN) RF generator in different parts of the endocardium for subsequent easy identification. In all of them a continuous unmodulated sinusoidal signal oscillating at 484.2 kHz was delivered in a temperature control mode limited to 80°C. Ninety minutes after the final application, the pig
was euthanized; the heart was excised and visually examined to identify the lesions. Sections of each lesion were obtained, fixed in 10% formalin, and stained with hematoxylin and eosin for a posterior histopathological study.

Results

In vitro contact and tissue evaluation

Once the catheter is introduced into the blood bath, the first reflection comes from the interface between blood and optic assembly denoted by B in Figure 2a,b. After the first interface, light is scattered strongly by the fluid. When the catheter tip approaches tissue, several reflections appear due to the complex structure of myocardium tissue. In the case of catheter approximation to the myocardium, corresponding to around 30 μm from the surface, a thin film of blood sits in between the tip and the endocardium. Consequently, the amplitude of the reflected signal in the first tissue layer decreases. In contrast, when the catheter is in direct contact with the myocardium the infrared light goes directly to the tissue, resulting in higher contrast in the structural signal (Figure 2b) and PR (not shown). In a separate capture, after 12 s of stable contact in healthy tissue, the catheter was moved to a previously ablated area (Figure 2c,d). As expected, strong contrast in PR between orthogonal polarization states in the two regions was found due to collagen fiber denaturation. These results are crucial to assess lesion continuity, a key point required for complete PVI and increased efficiency of the procedure.

In vivo procedure guided by PS-OCR

Organ movement complicates catheter access and reliable in vivo treatment. The high axial resolution of the structural image and the PR images allow identification of healthy tissue in front of the catheter (Figures 3 and 4). Stability of the contact against the endocardial wall due to heart beating could be assessed in real time (Figure 3a,b). A stable heartbeat of 102 bpm is observed as a slight oscillation in the contact distance to the endocardium, as well as the mechanical ventilation transmitted to the heart at a rate of 13 per minute (highlighted in Figure 3 with a sinusoidal plot for easy of visualization). After 31 s of imaging, with stable contact in the endocardial surface of the right ventricle, temperature-controlled RF energy was delivered for 60 s, with a target temperature of 80°C. The procedure was successful with respect to transmurality, as confirmed by histopathology of the lesion (Figure 3c), revealing observable microscopic alterations.
with signs of coagulative necrosis (Figure 3d). Similar results were obtained in the left atrium (Figure 3e,f). The electrical and optical details of the procedure are represented in Figure 4. Untreated swine myocardial tissue exhibits significant PR, while the birefringence properties disappear after applying enough RF energy, providing a strong source of contrast during lesion formation. The denaturation of collagen fibers happened 2 s after RF application, and the fiber denaturation time interval was around 1 s. A total of eight lesions were performed in different areas of the myocardium under fluoroscopy guidance distributed in such way that they could be clearly identified afterwards for further histological analysis.

Discussion

There is a relatively high incidence of recurrences in the RFA procedures after initially successful therapies. Contrast-enhanced magnetic resonance imaging studies with late gadolinium enhancement show that up to 20% of the RF applications guided by navigation systems do not translate into reliable lesions.15 To date, application of RF energy has been guided using indirect measures, such as impedance, tip temperature, or electrograms, but it has been demonstrated that the correlation of those parameters with lesion size is low.16,17 For those reasons, there is a strong clinical interest in developing new techniques to improve control over the ablation process. Others techniques, such as contact force18 or US have also shown limitations on the identification of ablated tissue. Recently a new design for an in vitro model has been implemented combining US and optics.19 While appreciating the potential of this technique for in vitro

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**Figure 2:** (a) Evolution of the structural image in time (M-scan mode) while the catheter is moved up and down in order to assess the proper contact between tip and myocardium tissue. Three situations are well defined: catheter approximation to myocardium (M-CA), blood (B), and myocardium direct contact (M-DC). (b) A single (A) scan of each of the three different stages. Phase retardation (PR) between orthogonal polarizations showing contrast between healthy and previously ablated tissue represented in M-scan mode (c) and mean phase retardation (MPR) in the 0.75–1 mm slice (d).

**Figure 3:** (a) Intensity M-scan of swine myocardium for in vivo model in the right ventricle. (b) Magnification of the shadow square to highlight the oscillation in catheter contact due to heartbeat and respiration. (c) Histological study of target tissue from the right ventricle stained with hematoxylin and eosin being appreciable in coagulative necrosis (cn), transition zone (tz), and healthy tissue (ht). (d) The microscopic image revealing signs of coagulative necrosis. (e) Intensity M-scan of swine myocardium in the left atrium. (f) Cross-section image of (e) with hematoxylin and eosin staining.
studies, we consider that this complex system is currently
difficult to implement in real therapies due to its mecha-
nical design and an independent guidance system.
Alternatively, a novel approach using endogenous nico-
tinamide adenine dinucleotide (NADH) fluorescence for
lesion assessment has been reported,20 but a potential
limitation of this is the strong attenuation of the
technology in the presence of even a thin blood film,
which might prove inconvenient in real cases.
In this paper, PS-OCR imaging integrated within an RFA
catheter has been demonstrated to be a potentially
clinically valuable technique with three main capabil-
ities: contact feedback, strong contrast allowing the
differentiation of healthy and ablated tissue, and real-
time monitoring of lesion formation. In particular, we
have observed that tip–tissue distance and contact can be
evaluated with high resolution. The strong contrast in the
polarization-sensitive signal provides a unique added
value during the ablation process, as tissue necrosis can
be linked to thermal denaturation of oriented collagen
fibers in the myocardium. This ability of PS-OCR is
crucial in order to confirm when RFA translates into an
effective necrotic lesion.
In this study, we have seen that changes in tissue due to
lesion formation can be observed in real time in the
optical signal. Quantitative evaluation of how the
acquired signals relate to the dynamics of tissue heating
and fiber shrinkage offers potential for improvement of
real-time lesion monitoring and accurate estimation of
lesion depth beyond the imaging range. The kinetic
nature of fiber denaturation is associated with a
modification of its mechanical tissue properties.21,22
Speckle cross-correlation or elastography seem like
appropriate techniques for further analysis of the tissue
mechanical deformations created by lines of necrotic
tissue.

Conclusion
We demonstrate that in vivo real-time evaluation of RFA
with PS-OCR using an integrated catheter is feasible. This
technique is a promising tool to guide RFA for
assessing catheter contact, monitoring lesion formation,
and differentiating between ablated and healthy tissue to
prevent gaps in a clinical setting. A limitation of this
study is related to the use of a single animal. Statistical
studies with several swine models that analyze long-
term outcomes will be required to corroborate the
results.
Additional work on lesion size prediction beyond the
imaging range can extend the clinical value of the
technique. Future technical developments will include
increasing the number of viewing directions and includ-
ing irrigation to maximize the clinical value of the device.
In the near future, PS-OCR-guided ablation has the
potential to emerge as a valuable tool for reducing
recurrence rates and adverse events, thereby improving
clinical outcomes and quality of life of the patients.

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