HHS Public Access

Author manuscript

Heart Rhythm. Author manuscript; available in PMC 2019 April 01.

Published in final edited form as:

Heart Rhythm. 2018 April ; 15(4): 576–577. doi:10.1016/j.hrthm.2018.01.003.

Lights On! Can Visual Light help distinguish fibrotic scars from ablation lesions?

Anuradha Kalyanasundaram, PhD[1] and **Vadim V. Fedorov, PhD**[1]

[1]Department of Physiology and Cell Biology, Davis Heart & Lung Research Institute, The Ohio State University Wexner Medical Center, Columbus, OH, USA;

Cardiac arrhythmias including ventricular tachycardia, ventricular fibrillation and the most prevalent rhythm abnormality, atrial fibrillation (AF), contribute and worsen functional outcomes in several cardiac diseases, often resulting in sudden cardiac death. Ablating targeted areas of abnormal electrical impulses is the mainstay of arrhythmia termination and to prevent the recurrence of future arrhythmic episodes. Several modalities including lasers, cryoablation and radiofrequency ablation (RFA) are used to treat sources of abnormal electric activity. RFA seeks to isolate highly arrhythmogenic areas by creating an irreversible fibrotic scar, which will be rendered electrically inactive thereby preventing arrhythmogenic electrical activity[1]. However, one of the main issues during clinical ablation procedures is distinguishing areas of permanently ablated lesions from electrically viable tissue missed during the procedure due to local edema; these transiently unexcitable areas may recover overtime and initiate abnormal electrical activation[2] which can lead to recurrent episodes of AF[1, 4, 5]. Hence there is a critical need to develop clinically relevant approaches, which can reliably estimate the distinct dimensions and locations of irreversible ablation-induced lesion/ scars as well as identify previous fibrotic scars.

At present, few imaging modalities are used to aid pre-surgery identification of target sites for cardiac ablation. Currently, advanced magnetic resonance imaging (MRI) is the only technique that can non-invasively identify atrial and ventricular fibrotic substrates and provide real-time assistance during the ablation procedure to track and position ablation catheters within cardiac chambers[3,4]. Unfortunately, clinical MRI has limited spatial resolution (up 1 mm^3) to effectively visualize transmural scar boundaries and identify viable tissue missed during ablation, especially in the atrial wall. In this scenario, catheter based techniques that can provide advanced visualization with submillimeter spatial resolution of myocardial fibrotic scars and RFA lesions could improve cardiac arrhythmia ablation outcomes.

In this issue of HeartRhythm, Swift et al[6] have investigated the utility of autofluorescence hyperspectral imaging (HSI) to identify and distinguish myocardial scar tissue from RFA ablation sites. HSI is a hybrid optical diagnostic technology, capable of obtaining spectroscopic information and delivering it in an image format[7]. Its unique strength is that it permits recording of the entire emission for each pixel across the entire image within the

Address for correspondence: Vadim V. Fedorov, PhD, The Ohio State University Wexner Medical Center, 5196 Graves Hall, 333 10th Street, Columbus OH 43210-1218, tel: 1-314-6004964, fax: 1-614-292-4888, vadim.fedorov@osumc.edu.

field of view, as opposed to conventional spectroscopy wherein the signal is recorded only at a single analyte location. As a result, HSI offers a veritable “data cube” of spectral description of the whole image at specific wavelengths[7]. HSI has found widespread utility to provide rapid *in vivo* diagnosis in varied disease conditions including cancer, arteriosclerosis and more recently in cardiac arrhythmias. HSI has been previously shown by the Sarvazyan group to be very effective in highlighting the contrast between ablated lesions and viable tissue[8] and to identify cardiac collagen based on its autofluorescence. Here, Swift et al[6] demonstrate using both *ex vivo* and *in vivo* rat heart models, that autofluorescence HSI can be effectively used to distinguish RF lesions and scar tissue at submillimeter spatial resolution. The main advantage of their approach is that autofluorescence HSI is based on distinct spectral changes in tissue autofluorescence unlike reflectance HSI, which is characterized by an increase in reflectance with no wavelength specificity. The data also show that the autofluorescence associated with HSI is marginally affected by blood in microcirculation in rat hearts, but will need to be validated in human hearts which have bigger coronary arteries and higher blood circulation.

Furthermore, Swift et al[6] elegantly demonstrate that HSI autofluorescence can identify collagen associated with scars which can help differentiate between sites of lesions vs. scars. This finding also suggests that such fluorescent catheters could potentially be employed to demarcate arrhythmogenic fibrotic regions, which harbor AF sources in diseased human hearts. Although the potential role of increased fibrosis in causing AF is widely accepted, clinically, a strong relationship between AF sources and fibrotic regions is yet to be established[9]. One reason for these controversial findings could be the lack of information regarding the intramural pattern and extent of fibrotic strands between cardiomyocytes in diseased hearts. Hence, imaging with visualization catheters that are equipped with high resolution capabilities such as HSI with a potential to interrogate sub-millimeter resolution would be a significant advancement to MRI based imaging data, to guide ablations and define fibrotic areas.

Although the demonstrated advantages of HSI are promising and justify further investigation, HSI has a long way to go before its technical hurdles are overcome and successfully employed in patients. It remains to be investigated as to how HSI would perform in *in vivo* beating human hearts to clearly differentiate scar associated collagen and lesion formation. Potentially, *in-vivo* endocardial surface HSI imaging data with inflatable balloon combined with percutaneous HSI visualization catheters could be used for endocardial surface recording, yet, the circulating blood would be expected to significantly affect HSI imaging with UV light. While the described studies could definitely be useful for imaging localized, surface areas, its capacity to determine scar tissue and differentiate lesions below the surface will require extensive testing in diseased *ex-vivo* human hearts and large clinically relevant animal models. Furthermore, inherent autofluorescence from cardiac tissue could play a critical role in determining the outcome of this technique as it varies greatly between animal vs. human hearts. Since most of the data presented by Swift et al[6] are from the ventricle, it also remains to be seen as to how this optical approach will work in atrial tissues. Moreover, the 3D muscle architecture of atrial fibers is very complex,[10] hence validating HSI in diseased human hearts would be required to confirm its applicability to aid AF related ablations. Additionally, HSI is an invasive procedure as opposed to MRI, which

limits its utility for longitudinal studies to track scar formation. For instance a recent canine study[5] shows that RFA lesions can be non-invasively imaged at regular intervals for 8 weeks using MRI to identify microvascular obstruction and regions of edema[5] which would be challenging for invasive catheter based optical studies.

Nevertheless, the authors should be truly congratulated for this exciting study. Going forward, development of specialized cardiac visualization catheters that could be incorporated with HSI capabilities will definitely improve non-invasive guidance for cardiac ablations. On a different note, this technology could also help deliver stem cells or adenoviral based therapeutic proteins/drugs to highly targeted sites, in association with other imaging modalities such as cardiac MRI. Future studies should focus on validating these novel applications of HSI in *in vivo* beating hearts and potentially in concert with MRI in order to calibrate this innovative optical approach for human applications.

Acknowledgments

Sources of Funding: This work was supported by NIH R01 HL135109 and American Heart Association Grant in Aid #16GRNT31010036 (VVF)

References

1. Calkins H, Hindricks G, Cappato R et al. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation. HeartRhythm 2017;14:e275–e444.
2. Ouyang F, Tilz R, Chun J, et al. Long-term results of catheter ablation in paroxysmal atrial fibrillation: lessons from a 5-year follow-up. Circulation 2010;122:2368–2377. [PubMed: 21098450]
3. Kim RJ, Fieno DS, Parrish TB et al. Relationship of MRI delayed contrast enhancement to irreversible injury, infarct age, and contractile function. Circulation 1999;100:1992–2002. [PubMed: 10556226]
4. Nazarian S, Kolandaivelu A, Zviman MM et al. Feasibility of real-time magnetic resonance imaging for catheter guidance in electrophysiology studies. Circulation 2008;118:223–229. [PubMed: 18574048]
5. Ghafoori E, Kholmovski EG, Thomas S et al. Characterization of Gadolinium Contrast Enhancement of Radiofrequency Ablation Lesions in Predicting Edema and Chronic Lesion Size. Circ Arrhythm and electrophysiol 2017;10:e005599.
6. Swift LM, Asfour H, Muselimyan N, Larson C, Armstrong K, Sarvazyan NA. Hyperspectral imaging for label-free in vivo identification of myocardial scars and sites of radiofrequency ablation lesions. HeartRhythm 2017 in press.
7. Vo-Dinh T, Stokes DL, Wabuyele MB et al. A hyperspectral imaging system for in vivo optical diagnostics. Hyperspectral imaging basic principles, instrumental systems, and applications of biomedical interest. IEEE Eng in Med & Biol mag 2004;23:40–49. [PubMed: 15565798]
8. Muselimyan N, Swift LM, Asfour H, et al. Seeing the Invisible: Revealing Atrial Ablation Lesions Using Hyperspectral Imaging Approach. PloS one 2016;11:e0167760. [PubMed: 27930718]
9. Hansen BJ, Zhao J, Fedorov VV. Fibrosis and Atrial Fibrillation: Computerized and Optical Mapping; A View into the Human Atria at Submillimeter Resolution. JACC Clin electrophysiol 2017;3:531–546. [PubMed: 29159313]
10. Zhao J, Hansen BJ, Wang Y, et al. Three-dimensional Integrated Functional, Structural, and Computational Mapping to Define the Structural “Fingerprints” of Heart-Specific Atrial Fibrillation Drivers in Human Heart Ex Vivo. JAHA 2017;6:e005922 [PubMed: 28862969]