EDITORIAL COMMENTARY

Ultrasonic measurements of local activation times: Toward the realization of a clinical intramural cardiac electrical mapping?

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Starting from the early 1930s with pioneering studies such as those by Barker et al., the mapping of the surface local activation times of the human cardiac tissue, i.e., the local timings of the excitatory process, has been a key element in electrophysiological studies aimed at identifying arrhythmogenic sources. In common clinical procedures, this is usually achieved invasively by measuring the local electrograms using epicardial or endocardial contact leads. Aside from the clinical and financial drawbacks of an invasive catheterization surgery, the important information regarding the intramural electrical activity can only be loosely inferred from the surface measurements and thus remains largely unknown. Three dimensional (3D) mapping of the cardiac electrical activity has so far been preliminary and experimental, and mostly inapplicable to intact hearts. Although arrays of plunge electrodes can be used to map the instantaneous distribution of the excitatory process in the 3D cardiac tissue, this technique suffers from substantial technical limitations, is restricted to isolated hearts, and therefore cannot be applied in surgery. Recent attempts to perform 3D cardiac mapping include trans-illumination, whereby the subendocardial and subepicardial electrical activity can be accessed via optical mapping in combination with photon diffusion theory, yet this technique is relevant only to thin tissues, requires toxic dyes, and can only be applied in laboratory setups. A major step toward a clinically feasible noninvasive mapping of the cardiac electrical activity is the electrocardiographic imaging method, which involves the solution of a highly ill-conditioned inverse problem, thus providing relatively low spatial resolution of the activation waves, and which is highly sensitive to noise. Additionally, it requires an auxiliary imaging modality that either utilizes ionizing radiation (e.g., X-ray computed tomography) or is costly (e.g., magnetic resonance imaging). Nevertheless, electrocardiographic imaging has been shown in preliminary research to be clinically informative to some extent and is still under validation studies.

Despite the ongoing efforts to map the cardiac 3D electrical excitatory process, no satisfactory technologies have yet to be found clinically apt. As an alternative, cardiac elastography, in which the cardiac tissue regional strain is measured using a high-frame-rate ultrasound, has been recently proposed by some research groups as a correlate to the direct measure of the electrical conduction. The cardiac tissue exhibits a well-known excitation–contraction coupling, i.e., under normal conditions a mechanical contraction wave follows the electrical excitatory wave within a few milliseconds of delay. Therefore, with the recent capabilities of ultrasonic machines to measure regional strain and strain rate of the cardiac tissue with sufficiently high spatial and temporal resolutions (>200 frames/s), one can perform the so-called electromechanical wave (EW) imaging and infer the local electrical activation times from the local, small deformations in the myocardium. This technique is noninvasive, and can provide intramural information of strain from any desired echocardiographic viewing angle. Preliminary works on animal and human models have shown the high potential of the technique to measure electrical attributes of the excitatory wave, e.g., its velocity and pacing origin, as well as to distinguish ischemic from normal regions in the heart. However, the intuitive correlation between the spatiotemporal dynamics of the electrical and mechanical waves could not be proven experimentally with contemporary methods because the electrical wave cannot be measured in a fine 3D resolution without the insertion of numerous plunge electrodes, which in turn interfere with the minuscule strains and the electromechanical wave itself.

In this issue of Heart Rhythm, Provost et al. used an integrative, state-of-the-art computerized model in conjunction with an in vivo experiment to provide for the first time, to the best of my knowledge, a solid support to the notion that electromechanical wave imaging can be used to represent the electrical activation wave. Using a commercial ultrasound system, they performed EW imaging on a mongrel dog undergoing ventricular pacing from 3 locations. By splitting the field of view into overlapping sectors and using advanced signal processing algorithms (including spatial cross-correlations and motion matching), they reconstructed full-view cine-loops of the interframe strains overlaid on the B-mode ultrasonic images. This unique automated composite technique allowed them to acquire strain images at an
impressive frame rate of 370 frames/s, which could be used to
detect very small (<0.025%) interframe displacements
and to generate isochrones with fine resolution. The in silico
model incorporated a magnetic resonance imaging–ex-
ttracted realistic anatomical model of a canine heart includ-
ing myocardial fiber orientation, and the finite-element
method was used to compute the electrical and mechanical
waves by solving the equations describing the coupled elec-
trical, mechanical, and circulatory system (both systemic
and pulmonary) components. Although different dog hearts
were used in the in vivo and in silico models, a notable
similarity in the interframe strain movies and EW iso-
chrones was demonstrated for the 3 pacing locations along
the total time interval of 200 ms. A quantitative analysis
showed high linear correlations of the total fraction of
activated (contracted) tissue at any time point ($R^2 > 0.98$),
as well as absolute time delays of <$5$ ms for any given
fraction, between the experimental and numerical models.
These positive results proved the relevance and predictive
power of the sophisticated integrative numerical model, and
enabled the authors to compare the simulated EW iso-
chrones to the simulated electrical activation times. For the
3 pacing protocols and for 2 clinically common imaging
angles, a strong linear relationship was found with slopes
$<1.17$ (correlation coefficients of $R^2 > 0.85$), and the
location of the pacing electrode was inferred from the EW iso-
chrones with an accuracy of approximately 5 mm.

The elegant study by Provost et al\textsuperscript{15} is important in
several aspects. (1) It further establishes the EW imaging as
a clinically feasible, robust, noninvasive, and nonionizing
modality for imaging the intramural mechanical activation
wave. With advanced signal processing algorithms, the au-
thors showed the feasibility of a commercially available
ultrasonic system to measure local interframe deformations
of $<0.025\%$ with a very high frame rate, and therefore it
was possible to conceptually relate them to the preceding
electrical activation wave due to the electromechanical
coupling in the cardiac tissue. Previous attempts to establish a
robust (without the need to solve an ill-posed inverse prob-
lem) and noninvasive myocardial activation mapping relied
on the acquisition of torso surface electrograms and used
the bi-domain theory along with the critical point theorem.\textsuperscript{16}
However, such a method reconstructed only epicardial maps. (2) Due to the lack of appropriate experimental meth-
odology, the authors have performed an in silico reciprocity
study and established a highly anatomically and biophys-
detailed numerical model of the coupled cardiac elec-
trical and mechanical activities. With this model, they suc-
ceded in showing a remarkable correspondence between the
ultrasonic interframe images and those simulated by the
numerical model. This demonstrates the potential power of
in vivo/in silico reciprocity studies in scenarios in which
technical limitations at the present time prohibit the con-
duction of more traditional experimental validation studies.
It should be noted however that this study is still prelimi-
nary and was conducted on a single normal heart and a
single numerical model, with a pacing protocol in which the
electromechanical coupling is known to result in a stable,
monotonic relationship between the electrical and mechan-
ical activation times. Surely, further validation must be
made for other scenarios including various heart geometries
and diseased hearts exhibiting activation patterns that may
compromise the electromechanical coupling, and with other
than the 2 selected (parasternal and apical) viewing angles.
Nevertheless, the study by Provost et al\textsuperscript{15} still stands out as
an extremely important and promising step toward the re-
alization of the long-needed clinical imaging modality of
the intramural cardiac electrical activity.

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