Wave-Mapping as a Guide for Ablation of Atrial Fibrillation
A Daydream?

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In this issue of Circulation: Arrhythmia and Electrophysiology, Carrick et al.1 publish an article entitled “Ablation of multwavelet re-entry guided by circuit-density and distribution: maximizing the probability of circuit annihilation.” The main objective of this study was to use a computer model of atrial fibrillation (AF) to evaluate the efficacy of linear ablation lesions on initiation and perpetuation of multiwavelet reentry (MWR). The computational model consisted of a flat 2-dimensional array of 80×80 electrically excitable cells connected via resistive pathways. Each cell of this cellular automaton generates an action potential when it receives sufficient current from neighboring cells and subsequently undergoes a period of refractoriness. The characteristics of each cell’s action potential were determined by several programmed parameters (such as upstroke velocity, repolarization duration, and restitution) and electrotonic current shifts occurring during the simulation. Seven different tissues were studied. One tissue was uniform, whereas in the others a short-wavelength patch of variable size and position was introduced (created by shortening the action potential duration and increasing the intercellular resistance). In each tissue, MWR was induced by high frequency stimulation, and the density and distribution of circuit cores were quantified by a custom algorithm. Ten ablation lesion sets with different degrees of circuit-density overlap were applied to each tissue, and the percentages of successful MWR induction and duration of each induced episode (lasting for ≥2 seconds) were determined as a function of ablation length. The overall results of these simulations showed that ablation at sites of high circuit-density was most efficient in decreasing reentrant duration. In contrast, ablation lines delivered at sites of low circuit-density increased the inducibility of MWR and did little to decrease the time-to-termination of MWR. This led the authors to conclude that “circuit-density maps provide a means to determine the most effective and efficient distribution of ablation lesions for treatment of AF.” And more explicitly, that “with a map of circuit distribution in a given patient, one can predict the effect of a particular lesion set on the inducibility and sustainability of MWR before delivering a single lesion.”

These rather bold conclusions of course raise the basic question to what extent computer simulations can be translated toward AF in humans of flesh and blood. To what degree is in silico tissue comparable with the structure and architecture of the atrial wall? And are the mechanisms of multwavelet reentry in the computer simulation the same as the mechanisms responsible for perpetuation of longstanding AF in patients? The authors themselves are aware of these cavats as they wrote, “Our studies were performed in a very abstract domain: flat 2D sheets of tissue. As such they demonstrate the general principles of wave dynamics and their response to ablation but do not reveal specific details that can be anticipated in human atria.” “Ultimate biological confirmation is essential, of course, and remains pending.” In another simulation study published one year ago, Gharaviri et al.3 compared the stability and dynamics of fibrillation waves in a single-layer versus a dual-layer computer model. In the dual-layer model, the rate of wave generation in each layer turned out to be twice as high as in the single-layer model, resulting in a higher number of coexisting waves (wave-density) and a higher stability of AF. In the dual-layer model, >40% of the fibrillation waves originated from breakthrough at one of the connection points between the 2 layers. On the basis of this, these authors advised, “As endo-epicardial dissociation and breakthroughs significantly contribute to the stability of AF, mathematical models investigating the perpetuation of AF or therapeutic interventions in AF need to implement this phenomenon.”

Is AF a 2-Dimensional Process?

In recent years, evidence is accumulating that persistent AF in patients with structural heart disease is a complex 3-dimensional problem.6–11 Although low-resolution mapping studies with multipolar basket catheters claim that the majority of clinical AF is attributable to the presence of a single large mother rotor,12,13 high resolution mapping performed during cardiac surgery has been unable to detect reentrant circuits.1–3 In a recent study from Australia, in only 3 of 18 patients, a transient rotational circuit was observed that survived not longer than just a few cycles.8 In a large still ongoing study in patients with induced and persistent AF, in whom all accessible epicardial areas are mapped (>1500 points/patient),7 to date not a single rotor could be found. So, if in diseased human atria reentrant circuits have such a short life-time, what then is the source of the numerous fibrillation waves that occupy the atria uninterruptedly for so many years? If one is willing to give up the linear thinking that has explained all other
cardiac arrhythmias (except fibrillation) so successfully, then the answer is obvious. If one envisions the atrial wall, not as a simple 2-dimensional sheet, but as a more complex multilayer of cells that are connected by a critical number of junction sites, it becomes clear that fibrillation waves can live forever without the need of any reentrant or focal activity.

In the Figure, we give an example of wave-mapping in a patient with longstanding persistent AF and mitral valve disease. At the left, 2 snapshots are shown, taken from the right atrial free wall and the area between the pulmonary veins, respectively. Each color represents a different fibrillation wave (sequence of appearance according to the rainbow) with arrows indicating the main trajectories of the waves. Number, size, and direction of propagation of these multiple wavelets constantly varied like in a kaleidoscope. Two types of fibrillation waves can be distinguished: (1) peripheral waves, entering the mapping area from outside (black arrows) and (2) epicardial breakthroughs (EBs), appearing inside the mapping area (white asterisks). In the wave-map of the right atrium, 4 of the 7 epicardial waves originated from endo-EB. In the interpulmonary vein area also, 4 breakthroughs occurred. In the right part of the Figure, the incidence and spatial distribution of EBs is plotted for the whole recording period of 12 seconds. Each asterisk indicates a breakthrough site, its size being proportional to the number of EBs occurring at that site. Although the number of EBs varied widely from patient to patient and from site to site, they could occur virtually everywhere at the epicardial surface, right and left atria alike. In a group of 24 patients with longstanding persistent AF, the overall median incidence of EBs was 2.75/cm² per second. Because EBs were widely distributed over the entire epicardial surface, the total incidence can be estimated as ≥100 EBs per second. Simultaneous endo-epicardial mapping in the goat model of persistent AF has provided direct evidence for a high degree of endo-epicardial dissociation after 6 months of AF.10–11 These studies also showed that an equal number of breakthroughs occurred at the endocardial surface.10 This means that in patients with longstanding persistent AF, during each second, the amazing number of >200 breakthroughs should occur at the endocardial and epicardial surfaces of the atrial wall. The presence of such a large reservoir of AF sources readily explains why atrial fibrillation is such a stable rhythm.

A Daydream?

Notwithstanding the abovementioned limitations of the computational studies of Carrick et al and the reservations we have with respect to some of their conclusions, we share their optimism that by gaining a better understanding of the perpetuating mechanisms of AF, we should be able to design more effective ablation strategies to restore and maintain sinus rhythm. However, the first prerequisite is that we know what the vulnerable parameter(s) is for perpetuation of AF. Is it the distribution of dominant AF-frequencies, atrial refactoriness, or degree of irregularity of AF-cycles? Is it the number of fractionated electrograms or presence of areas with slow or discontinuous conduction? Or is it the amount of intra-atrial conduction block and endo-EB? Or could it be something else? Detailed quantitative endo-epicardial wave-mapping during cardiac surgery in patients with and without persistent AF could answer these questions. Once we know what to look for, less invasive techniques such as catheter-based or body surface mapping14 can be developed to provide a detailed and accurate image of the distribution of the vulnerable parameter(s) of the substrate of AF. Such a diagnosis of the stage of development of the substrate of AF could determine which treatment modality is indicated. First of all, it can tell us whether in a given patient, palliative treatment would be a wiser choice. This will prevent unnecessary ablation procedures in patients who, most probably, will not benefit from it. In the others, the image of the electrophathological substrate of AF could be used as a guide to target the arrhythmogenic substrate more specifically. However, attempts to guide AF ablation by fractionation mapping15 or ablating sites with high dominant frequencies16 to date have not been generally adopted. That is why “you may say I’m a dreamer.” But as the article of Carrick et al clearly shows, “…I’m not the only one.” At this point in time, it must certainly still be considered a daydream to think that we could repair the electrophathological changes responsible for perpetuating mechanisms of AF.
for perpetuation of AF. But as John Lennon continued to sing, “I hope someday you’ll join us, and the world will live as one.”

Disclosures
None.

References

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