Artificial Intelligence-guided mapping of persistent atrial fibrillation: complementary to or better than the electrophysiologist?

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Artificial intelligence (AI) has a fascinating history. It all started in the 1940s and 1950s with foundational work by pioneers like Alan Turing, who proposed the concept of a universal machine that could simulate any computation. In 1956, the term "AI" was coined at the Dartmouth Conference. This marked the beginning of AI as a field. In the 1960s and 1970s, there was optimism about rapid progress in AI. Early successes, like the creation of algorithms for problem-solving and the development of the ELIZA program, which could simulate a psychotherapist, fueled this enthusiasm. However, in the late 1970s and 1980s, AI hit a period of stagnation, known as the "AI winter," due to the limitations of the technology of the time and reduced funding. The 1990s saw a revival with the advent of machine learning and the internet. The focus shifted to data-driven approaches. This period also saw the development of practical applications, such as IBM's Deep Blue, which defeated chess champion Garry Kasparov. The 21st century brought even more advancements. The development of more sophisticated machine learning techniques, like deep learning, and the availability of large amounts of data and powerful computing resources, led to significant breakthroughs. AI systems like IBM's Watson winning Jeopardy! and the development of autonomous vehicles are examples of recent achievements.[1]

Using the prompt "please give us a brief history of AI", the paragraph above was created by ChatGPT[1], an interactive software based on a large language model. Some of the details provided by the AI-based chatbot were unknown to the authors. Therefore, we verified the validity of the facts presented by the software. We believe this represents a simple example on how AI-based solutions can be complementary to human labor.

Modern technology has long since found its way both into clinical practice and medical research. In the field of cardiac electrophysiology, automated processing of data from various sources (e.g., a 12-lead ECG, cardiac imaging, three-dimensional high-density mapping or intracardiac electrograms) may support the evaluation of complex pathophysiological mechanisms or offer guidance for clinical decision making. Recently, there has been a growing interest in the evaluation of AI-based solutions such as deep learning. Examples include the identification of suitable patients most likely to benefit from cardiac resynchronization theraqpy[2] or the classification of complex intracardiac electrical patterns during catheter ablation of atrial fibrillation (AF)[3]. Machine learning may also be helpful for real-time, "live" interpretation of data gathered by a three-dimensional mapping system during catheter ablation. In a recent study, Seitz et al. introduced Volta VX1, an AI-based, expert-trained, real-time software for the mapping of persistent AF[4]. The Volta VX1 system is based on a machine learning software aimed at the automated identification of patient-specific electrogram patterns, i.e., multipolar electrogram dispersion.

In this issue of the *Journal* , Bahlke and colleagues report procedural and clinical outcomes of 50 patients undergoing catheter ablation of persistent AF, supported by the Volta VX1 software[5]. The majority of the patients included in the study had long-standing persistent AF, and almost half had undergone at least one prior ablation. During high-density mapping of the left and the right atrium with a multi-electrode catheter and a conventional three-dimensional mapping system, areas of electrogram dispersion were automatically detected and tagged by the software. In addition to standard pulmonary vein isolation, only areas identified by the Volta software were targeted for ablation. The endpoint of successful ablation was defined as termination of AF by conversion either to atrial tachycardia or sinus rhythm. Subsequent ablation of consecutive atrial tachycardia was performed to achieve sinus rhythm. All identified areas of electrogram dispersion were targeted, even if conversion occurred before completing the ablation protocol. When considered appropriate, the ablated areas were connected with each other or with anatomical barriers following a so-called "ablate and connect" strategy, in order to avoid iatrogenic creation of arrhythmogenic substrate. Catheter ablation was performed using a high-power short-duration protocol. The mean procedure duration was approximately 3 hours, and the mean radiofrequency ablation time was 29 minutes. The authors observed a mean 40-ms increase in AF cycle length during the ablation procedure (162 to 202 ms), and conversion of AF to atrial tachycardia or termination to sinus rhythm was observed in 12 patients (24%). Accounting for a blanking period of 6 weeks, approximately 40% of the patients were free from arrhythmia recurrence at 1 year following the first Volta VX1-supported catheter ablation (mean follow-up duration 1 ± 0.5 year). Atrial tachycardia was the most common type of recurrent arrhythmia.

The study by Bahlke and colleagues adds to the existing literature on algorithm-based mapping and catheter ablation of persistent AF. Previous studies, including those investigating the Volta VX1 software, have largely excluded patients with a maximum episode duration exceeding 1 year. However, a patient-specific, individualized approach to catheter ablation targeted at atrial substrate modification may have its greatest potential in patients with more advanced disease.

We believe the following aspects should be considered when interpreting the data presented by Bahlke and colleagues:

1) Long-standing persistent AF is commonly associated with severe alterations of atrial electrical and structural substrate characteristics. It is uncertain whether i) Therefore, the key questions are: do repetitive organized activation patterns still exist in this complex context and ii) whether and how they could reliably be identified. Even though AF termination was observed in approximately 1 in 4 patients in the study, the authors did not report the corresponding proportion of patients with long-standing persistent AF in this group. The patient characteristics suggest a wide distribution of the baseline duration of AF (mean 50 ± 54 months), ranging from 1 month to more than 16 years. It may therefore be intuitive to assume that AF conversion or termination during ablation predominantly occurred in patients with shorter baseline AF duration.

2) In consideration of the complex electrical and structural alterations associated with long-standing persistent AF, there may be endpoints other than AF termination that are potentially better suited to define the procedural success of catheter ablation. Modification of the atrial substrate(s) in the absence of a clearly identified arrhythmia mechanism may rather aim at i) facilitating previously unsuccessful electrical cardioversion, ii) the prevention of early re-initiation, iii) the maintenance of sinus rhythm to enable reverse atrial remodeling or iv) the prevention of subsequent atrial tachycardia. With the Volta VX1 approach used in this study (as with other electrogram-guided approaches), the majority of observed arrhythmia recurrence was due to atrial tachycardia. Subsequent atrial tachycardia frequently occurs after electrogram-guided ablation due to uncommon, non-macroreentrant mechanisms and often prompts an additional procedure. Alternatively, anatomical approaches (e.g., line-based ablation), with or without the consideration of individual structural alterations such as low voltage areas, may prove beneficial and potentially avoid atrial tachycardia subsequent to ablation of AF.

3) Some studies have associated procedural AF termination with a beneficial long-term outcome following catheter ablation[6]. In the era of more extensive ablation, it was not uncommon to accept significant damage to large areas of the atrium. On the other hand, a significant proportion of patients without termination does not experience arrhythmia recurrence. This particularly interesting population has not been well characterized thus far. Until today, there is no alternative procedural endpoint directly related to the arrhythmia other than AF termination. Furthermore, it remains uncertain whether or not to aim at more extensive ablation in the absence of termination. Complete ablation of all targets identified by a machine learning-guided software such as Volta VX1 may represent a suitable endpoint that deserves further investigation. Alternatively, specific electrophysiological patterns in response to ablation like prolongation of AF cycle length, changes in local activation gradients and arrhythmia organization may contain valuable information. It is conceivable that AI-guided interpretation of the entirety of such parameters may identify other candidate endpoints for catheter ablation of more advanced forms of persistent AF.

4) A potential advantage of the Volta VX1[4] system is the automated and reproducible identification of dispersion patterns during AF that, *per se* , can be replicated by an electrophysiologist. With other software-based AF simulation and mapping tools (e.g., the CardioInsight[7] and FIRM[8] mapping system), the operator is forced to rely on the software output, without the opportunity to reassess or verify individual parameters. We believe that in our field, AI may currently have its greatest potential in being complementary to AF mapping interpretation of the electrophysiologist.

Finally, the optimal approach to catheter ablation of long-standing persistent AF remains unknown. AI-guided solutions such as the Volta VX1 system may specifically contribute to a better understanding of the pathophysiology of more advanced forms of AF. An individualized approach to catheter ablation that is targeted at the underlying mechanism(s) may ultimately move the field forward. Adequately designed, randomized clinical trials are needed to demonstrate that technological advancements improve patient-important outcomes.

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