



Multi-Electrode Ablation Catheters for AF Ablation: Effective Reality or Elegant Experiment?

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Introduction

The landmark publication by Haissaguerre et al. in 1998 on ablation of PV foci to cure AF, has led the way for a global rise of pulmonary vein isolation for ablation for AF.¹ Nowadays in many centres this comprises half of all ablations performed. In 2007, a consensus document was published by Calkins et al.² on behalf of HRS and EHRA to provide guidelines on how to perform procedures and how to determine efficacy. This has led to a new appreciation of historical data, and more vigorous and longer-term evaluation of patients after ablation for AF.

Over the last decade many innovative technologies have been introduced to facilitate AF ablation procedures and improve results. However, the relative contribution of many of these innovations is difficult to assess since methods of follow-up and definitions of success have not been uniform, and randomized trials that compare different technologies are lacking. Innovations have mainly developed in two directions: A. improving irrigated single-tip ablation catheters to be used with more extensive real-time 3-dimensional navigation systems and remote robotic steering, and B. anatomically designed ablation tools for specific LA targets in combination with other energy forms.

The latter innovations are appealing because they step away from the multitude of technical equipment, and are referred to as “single shot” de-

vices aiming to simplify the approach to AF ablation. These include balloon-based catheters using either cryogenic ablation, or ablation with radiofrequency, high-frequency ultrasound, or laser energy, that are used by occluding or filling the PV antrum and then destroy the electrical connection to the LA in a circular or sequential manner. Another design uses a mesh of wires in a circular design which can be extended to connect to the PV antrum wall to perform pulsed RF tissue ablation. All these single-shot devices seem more or less feasible, although success rates and potential for complications vary. Currently, cryo-balloon ablation seems to have established itself as an accepted therapy. Alternatively, among these new technologies, multi-electrode catheter ablation with phased RF energy is the other new technology that has had a rather rapid commercial uptake and been a fast rising star. This manuscript provides an overview of the technology, the results obtained so far, and its merits and pitfalls that still be faced.

Multi-Electrode Catheter and RF Technology

This technology uses both a new catheter design and an alternative version of RF energy as energy source.³⁻⁵ Currently, 3 catheter types have been specifically designed for AF ablation. For the purpose of AF treatment, the Pulmonary Vein Ablation Catheter (PVAC) is used for PV isola-

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tion (Figure 5), the Multi-Array Septal Catheter for septum CFAE ablation, and the Multi-Array Ablation Catheter (MAAC) for CFAE ablation at other LA targets. These catheters have in common that they can be used for mapping and pacing purposes, and for ablation at all electrodes simultaneously. The electrodes are made of platinum, and are smaller with a surface area of 26% (MASC/MAAC) and 40% (PVAC) compared to a 4 mm tip catheter. Each electrode has a separate thermocouple giving temperature feedback to an individual subunit of the RF generator that continuously regulates the power output to the electrode, avoiding overshoot in temperature. The generator uses RF energy in a novel way, by providing duty-cycled alternating unipolar and bipolar current. The unipolar current flows between the electrodes and the backplate to create lesions that penetrate deeper into the tissue. The bipolar current flows between adjacent electrodes to create lesion continuity between the electrodes. With the decapolar PVAC (\square 25 mm) this results in a circular lesion. The MAAC catheter with 4 arms containing 2 electrodes creates a cross shaped lesion, while the 3-armed MASC containing 4 electrodes creates linear lesions along each arm. The RF energy is phased, which means that a power of 100W is delivered on the electrode for several milliseconds and then turned down again to allow for cooling. This results in a net power output of no more than 10W per electrode to reach a target temperature of 60°C. As an additional feature, the generator can mix the phase differences of the duty-cycled energy on individual electrodes in such a way that specific ratios of bipolar to unipolar energy can be obtained. The amount of bipolar RF energy is 80% at 4:1, 66% at 2:1, and 50% at 1:1 setting. The mean depth of the lesion will vary respectively from 3, to 5, to 7 mm according with this setting. Typically, in the thinner PV antrum region with the PVAC the usual ratio setting is 4:1 to avoid ablation of tissue outside the heart. At most other areas a 1:1 ratio is used with MASC and MAAC to create deeper lesions.

Experimental Data

Despite its rather quick uptake, there is little published experimental data on how the technology actually works. The paper by Wijffels et al.⁵ contains a combination of in vitro and in vivo animal

experiments. In 21 blocks of bovine myocardium immersed in a tissue bath, in vitro ablations were carried out with PVAC. An electrode-tissue contact force at 30 ± 5 g was applied for 60 seconds with a maximum temperature of 60°C for all five energy modes (bipolar energy only, 4:1, 2:1 and 1:1 bipolar:unipolar and unipolar only). Additionally, the thigh muscle preparation model was used to perform PVAC ablation. Lastly, chronic experiments were performed in pigs where PVAC ablation was performed at the SVC-RA junction, and after 1 week the animals were sacrificed and examined for lesion characteristics. The in vitro data showed that lesion depth varied from about 3 to 7 mm, as a function of using only bipolar RF energy to using increasing portions to only unipolar RF energy. While lesion length and width were not affected. Similar results were observed both in the thigh muscle preparations, and in vivo in the porcine SVC-LA junction. In the swine experiments, pathology showed that most lesions extended transmurally, while sometimes extracardiac effects were observed. In 3 animals small remote effects of the applications were seen at the aorta, lung, or atrial wall. One animal died directly after the procedure from non-cardiac cause, while in no animal perforation or necrosis was observed.

Acute Results and Long Term Efficacy

PV Isolation can usually be accomplished with a mean of 6 applications of 1 minute per vein by PVAC ablation in the antrum. The isolation may be verified by the usual techniques with a decapolar mapping ring catheter or the PVAC itself by pacing maneuvers, PV voltage analysis, or pharmacological challenge, similar to any other PVI procedure regardless of technology used.⁶⁻¹² In a group of 98 pts with PAF, the PVAC procedure time was 89 min with 18 min of fluoroscopy, with no procedural complications.³ Follow-up with 7-day Holter recording at 6 mos showed freedom from AF in 83% of pts. There are several published single centre registry results at 6-12 mo for freedom from AF with 2-day to 7-day Holter, showing an efficacy ranging from 60-90%.^{3, 13-17} Procedure time ranges from 85-120 min, while fluoroscopy time range from 18-40 min. Bulava et al.¹⁸ and Bittner et al.¹⁹ performed a single center randomized controlled clinical trial, comparing PVAC to conventional single-tip

catheter ablation with 3-D navigation. Both trials showed non-inferior efficacy for freedom from AF at around 9mo (PVAC 78%, single-tip 72%) while procedure (100 vs 200 min) and fluoroscopy (20-40 min) times were considerably shorter for PVAC.

In patients with (longstanding) persistent or accepted AF, there is abundant evidence that PVI alone is insufficient to achieve a reasonable efficacy for freedom from AF.²⁰ The highest reported efficacy comes from the group of Bordeaux,²¹ using a stepwise approach with PVI, lines at the LA roof and mitral isthmus, tricuspid isthmus, CFAE ablation, CS ablation, and sometimes SVC isolation to achieve freedom from AF in 50% of patients, increasing to 90% after up to 3 procedures to treat remaining arrhythmias. From the work of Nademanee et al.²² in 2004, ablation of complex fractionated atrial electrograms (CFAE) in the LA alone seemed to be a very promising approach. For this reason, the multi-arm, multi-electrode catheters MASC and MAAC were designed to target CFAE at the left inter-atrial septum, and the other walls of the LA. In the first clinical pilot multi-center study with this system.⁴ 50 patients with longstanding persistent AF were treated with PVAC and additional LA CFAE ablation with the MASC and MAAC catheter. Septum ablation typically required 8 MASC applications, and a mean of 13 applications were done with MAAC at the roof, posterior wall, MV isthmus and annulus. Acute efficacy with successful PVI, CFAE ablation and leaving in SR was achieved in 94% of patients. The total procedure time was 155 min with 55 min of fluoroscopy. A second procedure was performed in 50% of pts for early AF recurrence. At 6 mos, 7 day Holter showed freedom from AF in 70% of pts while in 10% AF transformed from chronic to paroxysmal without using drugs. At 20 mos the efficacy decreased to around 60%. Observed procedural complications included 2 groin vessel problems, 1 tamponade secondary to transeptal puncture, and 1 TIA with complete resolution. Recently, Mulder et al.²³ published single center results with a similar study design in a group of 89 pts with longstanding persistent AF. After a single procedure, freedom from AF without AAD or any other therapy, after 12 mo follow-up was 33%. Including an electrical cardioversion, and a redo procedure in 14% of pts, curing another 40% of these pts and increasing the efficacy of 52% at 12-mo follow-up. Of note,

in both studies LA flutter resulting from ablation were not observed, which is a striking difference with the stepwise ablation approach from Bordeaux²¹ where up to 50% of pts may show atypical flutter requiring additional treatment .

Safety of Phased RF Energy and Multi-Electrode Catheters

With any new technology for AF ablation, safety aspects are an important part of determining its value in clinical practice.²⁴ If we look at published data, they have mainly been concerned about efficacy to isolate pulmonary veins, and achieving freedom from AF. In the initial papers^{3, 13-17} on PVAC in PAF published so far, there were no adverse events reported. Only Scharf et al.⁴ using PVAC/MASC/MAAC ablation, reported 4 complications in 50 pts, consisting of a procedural stroke, 2 groin vessel problems, and a tamponade due to complicated transeptal puncture. Mulder et al.²³ using PVAC/MASC/MAAC in 89 pts described no procedural events, but observed an acute coronary syndrome and a TIA within 24 hours, a TIA at 1 mo, and a late progressive pericardial effusion requiring draining. Bulava et al.¹⁸ in a randomized trial did not observe adverse clinical events, either in the PVAC group or the CARTO conventional group. A similar trial by Bittner et al.¹⁹ showed one pt with transient ST-elevation with PVAC, and 2 pts with femoral vascular problems after CARTO. There have also been some case reports on PV stenosis²⁴, and even phrenic nerve damage²⁵ although this is a rare event

As there is no gold standard on safety of catheter ablation, it remains difficult to compare technologies. The Worldwide Survey and its update by Cappato et al.²⁴ provides one of the largest registries, showing adverse events in up to 4.5% of patients. From the initial data in small populations of usually no more than 100 pts, the safety profile seems non-inferior to conventional AF ablation.

Recently, several papers have focussed on the phenomenon of silent cerebral ischemia (SCI) on DW-MRI, in patients that had undergone AF catheter ablation.²⁵⁻²⁸ This phenomenon in itself is not new as it has been described in a variety of cardiovascular catheter and surgical inter-

ventions. The exact mechanism and long-term implication of SCI have not become quite clear from these studies. SCI is seen in over 35% of patients treated with phased RF, compared to only up to 10% of patients after irrigated tip ablation or cryoablation. This obviously raises concern about the safety of catheter ablation in general, and phased RF ablation in particular, despite the fact that so far significant longterm effects of SCI remain to be further determined.³¹⁻³² Recent work from Deneke et al.³³ showed that if patients with documented post-procedural SCI, were studied again after several weeks or months, 94% of all SCI lesions disappear, leaving only very few patients with lasting scar. Although this at least tempers our acute concerns, there is obviously a need to elucidate the mechanism, in order to reduce the incidence of SCI.

From Elegant Experiment to Effective Reality?

As can be derived from the above, multi-electrode ablation with phased RF energy has made it's first impact on catheter ablation treatment for AF. The first clinical studies show initial results that do not seem much different from conventional single-tip with 3-D navigation. New tools are usually designed to overcome shortcomings of existing technology, not to simply replace them. So far, the only real improvement that is consistent, is that PVI with PVAC seems to be more easy and quick with this technology. This in itself could help to make catheter ablation for AF more accesible to the general electrophysiologist, and the vast number of AF patients. However, for this technology to become a mainstream accepted therapy, there are many hurdles to overcome. From a basic technology standpoint, there is still much to learn about phased RF. How reproducible and durable is lesion formation in vitro and in vivo?^{34,35} Could we still improve lesion formation by changing electrode size and shape, or by using gold instead of platinum? How evolved is the concept of phased RF with regard to duty cycle and mixture of bipolar and unipolar energy? Could lesion formation be improved by better knowledge about contact by measuring impedance or force? Are all electrodes making enough contact with the tissue to create a lesion during an application? Do electrodes that are not in good contact with

the tissue create potential problems such as scar formation or thrombo-embolism? Is electrode cooling needed to overcome several issues that are similar to conventional RF catheters?³⁶ These are just a few of the questions that may require more study to understand and refine the technology.

Efficacy of PVAC PVI so far seems to be non-inferior to conventional ablation. Although this may seem sufficient, one would actually hope for an improvement in freedom of AF form a new technology. Aside from the technical issues discussed, other factors may be involved. So far, most studies have used 4:1 bipolar-unipolar RF energy for PVI, to refrain from very deep lesions out of safety considerations. There are no studies that have directly compared, efficacy and safety using 2:1 or 1:1 settings for ablation.³⁴ In patient that have undergone PVAC PVI but have a recurrence, mapping demonstrates that one or more PV show conduction to the LA. This may be due to failure to isolate the vein during the first procedure, as some studies using a circular mapping catheter show that small PV potentials may be missed in up to 10% when the PVAC itself is used to demonstrate PVI.^{6,9} Additionally, infusion of isoproterenol or adenosine may help to identify areas that have not been sufficiently ablated.¹² There may also be specific locations such as the LSPV-LAA ridge or the carina, that may be difficult to cover with the PVAC. It might be helpful to have some form of mapping as well as an indication of the local tissue thickness, to apply the PVAC at the right site with the right amount of energy.

With regard to the treatment of longstanding persistent AF with PVAC, MASC, and MAAC, there are still many questions to be answered. For the MASC and MAAC catheter, technical and strategic issues similar to those with PVAC require further study. These catheters were designed, building on the CFAE ablation strategy proposed by Nademanee et al.²² These catheters so far have been used in a random fashion, using visual qualification of fractionated LA potentials to guide ablation. Proper validation of the CFAE ablation approach is still being debated, and it is unclear to what extent MASC or MAAC ablation contributes to achieve freedom from AF. As there is no gold standard in longstanding persistent AF, additional studies are needed to determine the ablation targets and strategy.

Disclosures

The author currently is a consultant for Medtronic, Cameron Health. He was a former stockholder of Ablation Frontiers. He is a proctor for Medtronic and BScI/AtriTech. He has served on the speaker bureau for Medtronic, Boston Scientific, Biotronik, Cameron Health, and St.Jude Medical. The Cardiology Department received research grants from Medtronic, Boston Scientific, Biotronik, St.Jude Medical, Sorin/ELA, and AtriCure.

Conclusions

Multi-electrode ablation with phased RF-energy is feasible and initial data on efficacy and safety are promising. There is however concern about the high rate of silent cerebral ischemia that is observed. More studies are needed to better understand this very young technology, and to improve on technical aspects that may facilitate higher efficacy, and reduce unwanted side-effects even further. Larger randomized trials are needed, which shows long term outcome in comparison to other conventional ablation strategies. Only after such data becomes available we will be able to appreciate whether this technology has truly transformed from elegant experiment to effective reality

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