15

FUTURE INNOVATIONS IN CATHETER-BASED ARRHYTHMIA TREATMENT

Marco Perez, MD

Christopher Fellows, MD

EXECUTIVE SUMMARY

The recent increase in the demand for ablative therapy for atrial fibrillation fuels the development of more efficient and safer techniques. Robotic catheter manipulation will improve the stability, precision, and dexterity needed to perform long ablative procedures, and remote operation has the potential of limiting operator exposure to fluoroscopy. Novel catheters with balloon tips are being designed to more effectively perform circumferential lesions around pulmonary veins. Alternative energy sources such as microwave, high intensity focused ultrasound, laser, and cryotherapy each have distinct advantages and disadvantages that may prove useful in certain ablative approaches. With the ability to incorporate computed tomography or magnetic resonance imaging, mapping technologies will be able to more accurately localize catheters in three dimensions and superimpose electrical activation sequences onto cardiac anatomy with high resolution. The combination of these technologies will help decrease procedure times, minimize exposure to fluoroscopy, and achieve permanent destruction of precisely targeted tissue.

Introduction

The demand for ablative therapy has increased rapidly with the growing epidemic of atrial fibrillation (AF); however, current approaches to AF ablation are ineffective in approximately 20% of cases. In addition, these techniques are associated with certain risks, can be time-consuming, and are technically challenging. Emerging technologies strive to decrease procedure times, eliminate exposure to fluoroscopy, and achieve permanent destruction of precisely targeted tissue without damaging neighboring structures. These new technologies may eventually prove useful in the ablation of numerous other arrhythmias and will inevitably cross over to additional catheter-based interventions.

Robotic Catheter Manipulation

Ablation with conventional catheter manipulation has several limitations. Traditionally, motion of the tip of the catheter is limited to a single plane and a fixed radius of the catheter curvature. The difficulty of accessing tortuous vessels and structures at acute angles can add several hours to these procedures. The use of robotics in the surgical arena has brought greater stability, precision and dexterity to the operators as well as the potential for remote operation.

One such technology, Niobe® (Stereotaxis; St. Louis, MO), relies on a magnetic navigation system. A soft catheter with a small magnet-sensitive tip is manipulated by two large, external permanent magnets. With the use of a computer-controlled catheter advancing system, the catheter can be directed remotely (Figure 1). This system provides increased control of the catheter tip with freedom of motion in three dimensions. The ability to navigate remotely can significantly reduce operator radiation exposure. A recent series of 40 AF ablations using this system demonstrated successful remote ablation in 38 patients without complications and a short learning curve (1). The significant upfront cost of equipment installation, however, may be prohibitive to many smaller institutions.

Hansen Medical (Mountain View, CA) has developed a catheter control system that allows a remote operator to control catheters using electromechanical manipulation (Sensei™ Robotic Catheter System, Figure 2). The system consists of a master console with multiple video monitors and an intuitive motion controller joystick. Reports of early experience with humans demonstrated successful mapping of seven patients with atrial arrhythmias, ablation of two patients with atrioventricular nodal reentry tachycardia (AVNRT), and ablation of one patient with atrial flutter without complications (2).

Novel Catheter Designs

Electrical impulses from the pulmonary veins (PV) are considered to be an important, although not the only, trigger of atrial fibrillation. While PV isolation remains a goal in AF ablation strategies, successful circumferential lesions can often be difficult to make. Strategies to isolate the PV include the insertion of balloon tipped catheters, basket catheters, or circular catheters into the ostia of the PV to deliver various energy sources to complete ablation.

One such device is a balloon cryoablation catheter which uses cryothermal energy to isolate the PV. Early human studies demonstrated success rates of 75% using the balloon catheter alone and 95% when used in conjunction with focal cryocatheter ablation, without PV stenosis at 3 months (3). One of the major limitations is that success depends on direct contact of the catheter with the ostium of the PV. A catheter designed to overcome this limitation is the CardioFocus™ Endoscopic Laser Balloon Catheter (CardioFocus, Inc; Maynard, MA) (Figure 3). The catheter projects a series of overlapping arcs of visible and infrared laser light upon the atrial wall surrounding each pulmonary vein. With integrated endoscopic visualization, the operator confirms the desired location and delivers ablative light energy. In an early human study with five patients in AF, 89% of the PV were successfully accessed and complete circumferential contact was visualized with the fiberoptic endoscopic component in 15 of 16 PV accessed (94%) (4).

New Energy Sources

Radiofrequency ablation (RFA) has been used reliably for over 20 years to treat cardiac arrhythmias with acceptable safety. Therapeutic outcome is dependent on thermal injury of the target tissue by electric current-mediated heat. However, the delivery of RFA to deep or scarred tissue is difficult because of the risk of extensive superficial damage or clot formation. While cooling of the catheter tip with irrigation can overcome some of these limitations (5), several new energy sources are being developed to better target tissue ablation (Table 1).

Microwaves stimulate rapid oscillation of H_20 molecules and can heat a greater amount of tissue without damaging the endocardium. Although catheter-based applications have not been efficacious, its use in surgical Maze procedures has shown a 61% cure rate (6).

High-Intensity Focused Ultrasound (HiFU) results in tissue damage by cyclically expanding and shrinking microbubbles in tissue. Ultrasound beams can be focused at desired tissue depths and may prove useful in epicardial ablation due to its ability to penetrate beyond fat to deeper tissues. HiFU has shown great promise for epicardial limited surgical ablations (7) and is in the early stages of development for catheter-based application.

Laser beams are created by stimulating emission of radiation to produce light amplification. These beams cause vibration of molecules in tissue and the heat generated results in destruction of the target. Early intraoperative studies demonstrated successful ablation of ventricular tachycardia (8). A linear diffuser allowing for delivery of transmural lesions has been successfully used in animal models (9). More recently developed catheters have used a beam splitter to create laser balloons designed for pulmonary vein isolation.

Cryotherapy is performed by delivering precooled compressed gas to lower the temperature of the catheter tip below -75℃ which results in irreversible cellular injury. One major advantage of this technique is that the catheter tip adheres to the tissue and results in stable tissue ablation. The Freezor™ trial of Supraventricular Tachycardia (FROSTY) trial reported successful postablative suppression of AVNRT in 94 of 101 patients with excellent safety (10). Cell death, however, may not be immediate, and success may be difficult to assess during the procedure. A high rate of recurrence in early studies may be an additional limiting factor.

Mapping and Image Registration

The success of these catheter-based technologies depends on precise localization of the catheters being used. Although fluoroscopy has been used for several years, X-ray exposure during catheter ablation is associated with increased risk of "burns" and malignancy. Techniques to localize catheters in three dimensions and minimize exposure to radiation are being developed. Mapping technologies aim to accurately depict cardiac anatomy and superimpose electrical activation patterns.

The Carto™ XP Electroanatomical Mapping System (Biosense Webster, a Johnson & Johnson Company; Israel) uses a tripod that emits three electromagnetic waves at different frequencies. A specialized catheter tip with embedded coils registers these beams and is able to determine its location in three dimensions. The catheter tip is moved around the structure of interest, recording local tissue activation at each site to create an activation map. The Ensite NavX™ Navigation and Visualization Technology system (St. Jude Medical; St. Paul, MN) uses low level, separable currents injected from three electrodes on the body surface. Localization of a catheter tip is based on the three resulting potentials measured with respect to a reference electrode. Experience using these and other mapping systems for AF ablations continues to grow.

Part of the difficulty behind AF ablation is the significant variation in pulmonary vein anatomy. Although cardiac anatomy can be reconstructed using these mapping systems by recording the catheter tip at different locations, the resolution is highly dependent on the number of points collected and often over 50 points must be gathered to obtain accurate chamber geometry. Consequently, computed tomography (CT) and/or magnetic resonance (MR) image registration are increasingly incorporated into each mapping system. The chamber of interest can be manually isolated from a CT or MR scan and is then imported into the mapping system software. Using fluoroscopic landmarks as a guide, the high resolution scan is then aligned with the image obtained using the mapping system. Alternatively, the software can automatically create a best-fit between the imported scanned image and the image obtained using electromechanical mapping. Once the images are aligned, the activation map as well as the real-time position of catheters can be superimposed onto the imported CT or MR image with high spatial resolution. Using these registration techniques, ablative lesions can be delivered with greater accuracy. In a recent report with 30 patients undergoing AF ablation using CT image integration, registration was achieved with an error of approximately 6mm using fluoroscopic landmarks for alignment and about 2mm using the best-fit models (11).

Conclusion

The emerging technologies reviewed here will bring improved ease to currently challenging procedures, and in doing so will allow an increasing number of patients to benefit. The presence of competing technologies will inevitably push the field to contain cost and improve safety. Further experience with these new techniques and the clinical studies to validate their efficacy will be needed to determine which of these innovations will undergo widespread use.

Table 1. Advantages and Disadvantages of Various Energy Sources

Energy Source	**Advantages**	**Disadvantages**
Radiofrequency	- Significant experience - Established safety	- Requires direct tissue contact - Charring and tissue popping can occur; deep tissue modification difficult - Propensity for thrombus formation
Microwave	- Heat greater amount of tissue - Less endocardial damage	- Catheter-based applications unsuccessful
Ultrasound	- Increased depth of tissue damage - May be useful for epicardial ablation	- PVI attempts were unsuccessful
Laser	- Linear, transmural lesions are possible	- Insufficient contact may produce clot
Cryotherapy	- Less thrombogenic - Adherence results in lesion stability	- Temperatures highly variable - Cell death may be delayed - Risk of rupture or fistula formation

Figure 1. Magnetic Navigation: Stereotaxis Niobe® System

Photograph courtesy of and reproduced with permission from Stereotaxis, St. Louis, MO, USA

Figure 2. Electromechanical Navigation: Hansen Medical Sensei™ System

Photograph courtesy of and reproduced with permission from Hansen Medical, Mountain View, CA, USA

Figure 3. CardioFocus™ Endoscopic Laser Balloon Catheter

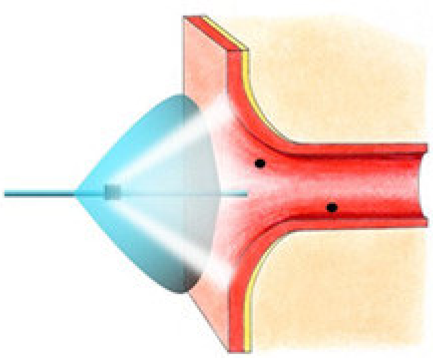

Image courtesy of and reproduced with permission from CardioFocus, Inc., Maynard, MA, USA

References

1. Pappone C, Vicedomini G, Manguso F, Gugliotta F, Mazzone P, Gulletta S, Sora N, Sala S, Marzi A, Augello G, Livolsi L, Santagostino A, Santinelli V. Robotic magnetic navigation for atrial fibrillation ablation. *J Am Coll Cardiol* 2006;47:1390-1400.
2. Thal SG, Marrouche NF. Novel applications in catheter ablation. *J Interv Card Electrophysiol* 2005;13 Suppl 1:17-21.
3. Doshi SK, Laragy M, Pitchner HF, Irwin J, Cole C, Neuzil P, Kuniss M, Ruskin JN, Reddy VY. The additive efficacy and safety of circumferential pulmonary vein isolation using a novel cryothermal balloon ablation system. Presented at the Heart Rhythm 2005 Scientific Sessions, New Orleans, LA 2005.
4. Themistoclakis S, Wazni OM, Saliba W, Schweikert RA, Bonso A, Rossillo A, Gordon M, Melsky J, Raviele A, Natale A. Endoscopic fiberoptic assessment of balloon occlusion of the pulmonary vein ostium in humans: comparison with phased-array intracardiac echocardiography. *Heart Rhythm* 2006;3:44-49.
5. Calkins H, Epstein A, Packer D, Arria AM, Hummel J, Gilligan DM, Trusso J, Carlson M, Luceri R, Kopelman H, Wilber D, Wharton JM, Stevenson W. Catheter ablation of ventricular tachycardia in patients with structural heart disease using cooled radiofrequency energy: results of a prospective multicenter study. Cooled RF Multi Center Investigators Group. *J Am Coll Cardiol* 2000;35:1905-1914.
6. Knaut M, Tugtekin SM, Spitzer S, Gulielmos V. Combined atrial fibrillation and mitral valve surgery using microwave technology. *Semin Thorac Cardiovasc Surg* 2002;14:226-231.
7. Ninet J, Roques X, Seitelberger R, Deville C, Pomar JL, Robin J, Jegaden O, Wellens F, Wolner E, Vedrinne C, Gottardi R, Orrit J, Billes MA, Hoffmann DA, Cox JL, Champsaur GL. Surgical ablation of atrial fibrillation with off-pump, epicardial, high-intensity focused ultrasound: results of a multicenter trial. *J Thorac Cardiovasc Surg* 2005;130:803-809.
8. Saksena S, Gielchinsky I, Tullo NG. Argon laser ablation of malignant ventricular tachycardia associated with coronary artery disease. Am J Cardiol 1989;64:1298-1304.
9. Keane D, Ruskin JN. Linear atrial ablation with a diode laser and fiberoptic catheter. *Circulation* 1999;100:e59-60.
10. Friedman PL, Dubuc M, Green MS, Jackman WM, Keane DT, Marinchak RA, Nazari J, Packer DL, Skanes A, Steinberg JS, Stevenson WG, Tchou PJ, Wilber DJ, Worley SJ. Catheter cryoablation of supraventricular tachycardia: results of the multicenter prospective "frosty" trial. *Heart Rhythm* 2004;1:129-138.
11. Kistler PM, Earley MJ, Harris S, Abrams D, Ellis S, Sporton SC, Schilling RJ. Validation of three-dimensional cardiac image integration: use of integrated CT image into electroanatomic mapping system to perform catheter ablation of atrial fibrillation. *J Cardiovasc Electrophysiol* 2006;17:341-348.