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Differences in Tissue Injury and Ablation Outcomes in Atrial Fibrillation Patients – Manual versus Robotic Catheters

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Abstract

Robots have gained their place in almost all areas of our daily life. Robotic systems have been introduced for ablation therapies associated with the hope of automation of procedures, increase in precision of lesion placement, improved energy transmission to the tissue and reduction in radiation exposure of the patients and the interventionalist. Finally, they may be associated with higher comfort for the operator by transferring his work into the control room and thereby supersede wearing sterile and radiation protective clothing. Systems providing a remote mechanical replacement of the operators´ hands have been introduced as well as systems guiding the catheter tip by external magnets. Guiding of the catheter tip has major impact on contact to the tissue and thereby modifies energy transmission. This may be advantageous in terms of higher catheter stability and modification of contact towards a more constant than intermittent type of contact. However, increasing contact bears the risk of mechanical perforation and excessive energy delivery. Many clinical studies have been conducted evaluating novel remotely guiding techniques in atrial fibrillation ablation procedures. Although only a few of them are prospectively randomized, reduction in fluoroscopy exposure has been found in most of the trials. Data on outcome is less uniform. It seems that remote navigation does not improve outcomes and on the other hand does not increase complication rates. However, large prospectively randomized trials conducted by operators well skilled not only in manual but also in remote techniques would be needed to compare outcomes particularly in terms of decrease in complication rates. Finally, the type of navigation chosen actually is and probably will remain a question of personal preference.

Introduction

Ablation therapy is an established second line treatment option in patients suffering from atrial fibrillation (AF). Most recent guidelines opened the door to first line treatment of paroxysmal AF instead of passing through an attempt of unsuccessful antiarrhythmic drug therapy.[1] Although cryoenergy has gained in importance radiofrequency (RF) energy still is the predominant source of energy. Many ablation strategies have been introduced for RF ablation of AF for more than a decade. However, the success rate falls short of 100% and a relevant proportion of complications is a matter of concern. Recurrences of AF after ablation may be traced back to many factors including patient selection, ablation strategy, skills of the operator and others. Finally it all comes back to the need for creation of a durable lesion at the right spot. Therefore, optimization of lesion formation has the potential of improving the outcome of AF ablation. As a consequence, attempts have been made to improve energy delivery to the tissue by using variable energy levels titrated by intracardiac echo, cooling the catheter tip and modification of the catheter tip in terms of configuration and material. However, evaluation of consistence of lesions in invasive follow-up studies still leads to unsatisfying results.[2] Two promising strategies have recently been introduced to improve contact between catheter and tissue and thereby increase effectiveness of energy delivery. One is to guide ablation by catheter feedback on contact force and lesion formation parameters. The other is to take the catheter out of the operator`s hands and to integrate it into remotely controlled machines promising optimization of catheter stability and type of contact. In principle, two different so called "robotic systems" are currently in use, one is the remotely controlled mechanically driven system (Sensei™ Robotic Catheter System, Hansen Medical, Mountain View, CA). The other system directs a special catheter embedded with 3 magnets by two external magnets creating a variable magnetic field and an additional external motor drive (Niobe™ ES, Stereotaxis St. Louis, MO).

Principles of Lesion Formation in Radiofrequency Current Ablation

Basically lesion formation is achieved by tissue overheating as an effect of RF current application to resistive tissue (resistive heating) in a process similar to what is happening in a light bulb. Resistive heating is proportional to the power density and decreases with the distance to the catheter tip describing an exponential decay.

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None.

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Therefore, only a small area around the catheter tip is heated directly and heating of tissue further away from the catheter tip is achieved by conductive heating also decreasing with the distances to the catheter tip. Thereby, areas close to the tip heat up quickly and deeper heating requires prolonged application times. As a tissue temperature of 50° C is needed to create persistent lesions the lesion size of a single application is always limited to the distance of a 50° C isothermal boundary reached during steady state of heating. Theoretically larger tips and higher power levels increase lesion sizes by means of increasing resistive and conductive heating. However, the level of power is limited by the temperature at the tip-tissue interfaces where overheating results in coagulum and thrombus formation leading to disruption of energy transmission. Irrigated tip catheters have been invented to overcome the issue of overheating at the tip-tissue interface and may result in greater lesion sizes compared to temperature controlled ablation.[3,4] However, excessive intramural heating bears the risk of "steam pops" and thereby may result in increased rates of perforation and tamponade. In addition to active cooling by open or closed irrigation of the catheter tip passive cooling is present when circulating blood cools the tip of the electrode and the interface between the tissue and the tip of the catheter. This type of convective cooling can be increased by use of larger electrode tips.[5] However, due to distribution of energy delivery between blood and tissue and the proportion of the catheter tip which is in contact to the tissue larger electrodes may also inversely result in smaller lesions in comparison to catheters equipped with smaller electrode tips.[6,7]

Given the catheter is well targeting the arrhythmogenic substrate, success of ablation depends on optimal lesion formation. Various factors influence lesion size by modifying the amount of power delivered to the tissue. Of importance are: power settings of the radiofrequency generator, electrode temperature (in particular in non-irrigated catheters), duration of energy delivery, impedance of the ablation circuit, electrode radius and geometry, active and passive cooling, size and position of the remote electrode, tissue properties, electrode material and last but not least stability of contact and contact force in between the electrode and the tissue.

Robotic Navigation Systems

Sensei Robotic Navigation System

The technology has been described before.[8-10] Briefly, Sensei™ robotic navigation system (Sensei™) (Hansen Medical, Mountain View, CA, USA) is an electromechanical system. Navigation is facilitated by means of two steerable sheaths (Artisan™/Lynx™ Hansen Medical, Mountain View, CA, USA) carrying the ablation catheter. The sheaths are fixed in a mechanical steering tool mounted on a robotic arm at the patients table. Outer sheath diameter is 14 F. Commands given by the operator are transferred from his remote workstation to the robotic arm making it follow intuitive movements of his hand. The system is equipped with a technology (IntelliSense™ Hansen Medical, Mountain View, CA, USA) providing a continuous visual feedback on contact force at the catheter tip.

Amigo™ Remote Catheter System

The system manufactured by Catheter Robotics, Inc., Mount Olive, NJ is mounted on a bridge over the patients legs. Electrophysiologic catheters are fixed on a docking station which allows for remotely directed catheter manipulations by a wired controller. The system is overall more simple than the Sensei™ and does not integrate any type of imaging technology. However, no additional sheath is needed and the system can be easily moved between different labs.

Magnetic Navigation Systems

Feasibility and safety of the Niobe™ magnetic navigation system (MNS, Stereotaxis, St. Louis, MO, USA) has been initially described by Faddis et al. in an animal model and Ernst et al. in ablation of supraventricular tachycardia.[11,12] During the following years it has been adopted for many types of arrhythmias, in particular for ablation of AF. The technological aspects of the system have been described before.[11-13] In brief, a catheter equipped with three magnets is guided by an external magnetic field created by two permanent magnets on the left and right side of the patient. Moving the magnets alters the magnetic field and thereby changes the orientation of the catheter. Forward and backward movements of the entire catheter are generated by an external motor drive. Movements of the external magnets and the motor drive are controlled remotely from the control room by the operator using a joy stick and/or a computer mouse. The system also allows for remote control of the circumferential mapping catheter,[14] the intracardiac echo catheter and the sheath carrying the ablation catheter (Vloop™, Vsono™, Vcath™, Stereotaxis St. Louis, MO). In the most recent version of the system (Niobe™ ES, Stereotaxis St. Louis, MO) an immediate response of the magnets to changes of the vector displayed and directed by the operator is realized. In conjunction with Carto 3 RMT™ (Biosense Webster, Diamond Bar, CA, USA) an automatic targeting of points on the surface of the anatomical map and the circumferential mapping catheter is possible (Figure 1). The system also gives feedback on the contact force between the catheter tip and the tissue.

An alternative magnetic navigation system called the "Catheter Guidance Control and Imaging Magnetic Navigation System" (CGCI MNS) (Magnetecs, Inglewood, CA, USA) has recently been introduced. The main difference to the established technology is the type of magnetic power used by the system. While Niobe™ uses two permanent magnets being moved themselves to change the configuration of the magnetic field, this system applies magnetic power of eight electromagnets arrangeed arounf the chest of a patient creating a dynamic magnetic field. Thereby, changes in the magnetic field can be achieved rapidly. Moreover, an obstacle-avoiding technology is integrated. The system is incorporated with a 3D mapping system (EnSite NavX, Sylmar, CA, USA).

Impact of Remote Navigation on Lesion Formation

In principal robotic navigation may have two kinds of impact on lesion formation. One is the increase of catheter stability, the other one is modification of contact force. This is true for all of these systems. While the mechanic systems (Sensei™, Amigo™) are capable of integrating customary ablation catheters, specialized magnetic catheters are required for the magnetic systems. Therefore, there might be an additional impact on lesion formation by the different kind of catheters used in the MNS.

Magnetic Navigation Systems

Experimental data on magnetic navigation compared to manual navigation reveals a significantly increased stability of the catheter tip at the same applied force. Moreover, the volatility of contact force seems to be higher in manually guided catheters.[15] This appears to be logical due to different types of forces applied to the catheters. In a manually directed catheter, force is applied by pushing it towards the

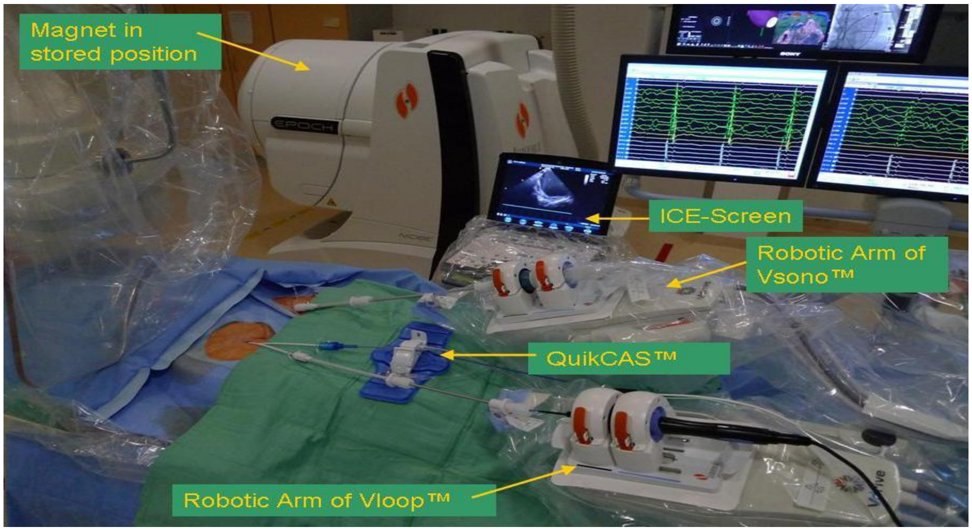

Figure 1: Magnetic Navigation System (Stereotaxis EpochTM) in a most recent set-up. One of the two magnets is displayed in a stored position. The intracardiac echocardiography (ICE) catheter is directed remotely by VsonoTM technology. A motor drive (QuikCASTM) is pulling and pushing the magnetic ablation catheter. Remote control of the circumferential mapping catheter fixed on a robotic arm is provided by VloopTM technology (Stereotaxis, St. Louis, MO).

tissue or rotating it against the wall. In contrast a floppy magnetic catheter is pulled towards the targeted wall and the constant magnetic field allows it to follow the movements of the beating heart in a certain range. Knowing that the type of contact is also relevant for sufficient lesion formation [16] it is conclusive that equivalent lesion sizes can be achieved at the same energy levels with lower contact forces using a magnetically navigated catheter.[15] However, contact force in magnetically guided catheters is limited by the maximum force resulting from the interaction of the magnetic fields of the catheter and the external magnets. This may be an advantage and a disadvantage at the same time, as increased contact force is likely to increase lesion sizes and probably also durability of lesions. However, increased contact force bears the risk of mechanical perforation[17] and exceeding forces of 20-30 g is associated with increased rates of "popping" and crater formation [18] both likely to increase the risk of perforation and tamponade.

Sensei™ Robotic Navigation System

Although comparative data on lesion formation in Sensei™ guided and manually guided ablation is missing, we got nice insight into lesion formation in procedures guided by Sensei™ from Di Biase et al.. They systematically evaluated the relationship between catheter forces (as measured by Intellisense™) lesion characteristics and side effects using the Sensei™ in an animal model.[18] Their findings reflect the complexity of the lesion formation process as discussed earlier. At 30 watts (W) lesions were more likely to be transmural at higher contact forces (>40 g) than lower pressures. However, a significantly higher number of lesions at this force showed severe side effects and a majority of lesions placed using higher power (45 W) with higher pressures (>40 g) were associated with char and crater formation although an open irrigated tip catheter was used. On the other hand side lesions placed with a power setting less than 35 W were more likely to result in relative sparing of the endocardial surface regardless of the pressure. The results shed light on a general dilemma in lesion formation: the higher power and contact force, the higher the rates of side effects, and the lower power and contact force, the lower the proportion of transmural lesions. However, an optimal level of contact pressure between 20 and 30 g and a power setting of 40 W was found to achieve transmurality at a preserved level of safety. Interestingly no lesions using 10 g of pressure were transmural regardless of the power. This might possibly be due to the increased stiffness of the whole system when the catheter is incorporated into two sheaths. This may lead to a different contact force volatility in terms of a more variable than constant type of contact being likely to reduce effectiveness of energy transmission.[16] Since then more refined parameters have been introduced evaluating not only contact force for prediction of lesion formation but also force-time integrals and energy transmission to the tissue estimated by current flow and impedance generating a lesion size index better reflecting the true size of the lesion (TactiCath Quartz™ force sensing ablation catheter system, Endosense, Geneva Switzerland). Although prospective human data on this novel parameter is not yet available animal data and retrospective analysis of a cohort of patients treated with a manual directed contact force catheter (Tacticath™, Endosense, Switzerland) are encouraging.[19] Integration of this technology into Sensei™ should be easy and may further improve monitoring of energy delivery.

Impact of Remote Navigation on Clinical Outcome

Magnetic Navigation Systems

During the last six years multiple studies have been published reporting on clinical outcome of patients undergoing magnetically guided ablation applying the Sensei™ for treatment of AF.[13,20-29] Three of these studies have been performed using a 4 mm non-irrigated catheter and therefore do not fully reflect the current approach.[13,20,21] Of these the study of Katsiyiannis et al. made a comparison between manually guided and magnetically guided procedures and found a comparable clinical outcome but significantly lower procedure and fluoroscopy times in the magnetically guided procedures. Taking into consideration that the power setting in the manual group had been even more aggressive, this is a remarkable result not reproduced by any of the following studies using different types of catheters.

Katsiyiannis et al. do not report on total ablation times but use of an 8mm tip catheter in the manual group may have had a negative impact on lesion formation in case a predominantly perpendicular orientation of the catheter had been chosen[6,7] and thereby may have led to prolonged procedures. In a recently published meta-analysis of 6 studies Bradfield et al. report on statistically better acute success rates for manual ablation.[30] However, this did not result in any difference in mid-term outcome and therefore seems to be of limited clinical relevance. In their meta-analysis of procedural data Bradfield et al. find trends towards longer procedure times, shorter fluoroscopy times and longer ablation times with the MNS. However, none of these differences reached a level of significance. Our own data comparing contact-force guided and magnetically guided ablation in a match-pairs fashion showing comparable clinical outcome in mid-term follow-up also finds a trend towards longer procedure times and significantly longer ablation times for the magnetic group [31] seems to be in line with the meta-analysis of Bradfield et al.

Data recently published by Lüthje et al. reporting on a large series of patients support the findings of the meta-analysis in terms of no differences in outcome. However, in their cohort use of magnetic navigation was associated with significantly longer procedure and ablation and significantly shorter fluoroscopy times.

Like many others they fail to prove any difference in complication rates.[28] However, Bauerfeind et al. report on a significant reduction in particular in terms of major complications in a mixed cohort treated with the MNS compared to manual navigation.[27] In summary, MNS is unlikely to reduce procedure and ablation times, however it has the potential to reduce total fluoroscopy times and in particular radiation exposure to the operator. Most of the studies included the learning curve of the operators and results therefore are not representative for routinely clinical application of the system. Prospective randomized data evaluating magnetic navigation for ablation of AF is lacking.

Data on the CGCI MNS is limited to a report on early experience in an animal model.[32]

Sensei™ Robotic Navigation System

The system has been evaluated in several studies.[10,33-40] Reddy at al. reported on 9 successful AF ablation procedures in humans after a training in only 9 animals.[33] This was followed by a multi-center study published by Saliba et al. in 40 AF patients confirming the results in terms of a 100% success rate in isolation of the pulmonary veins. Moreover, they found freedom from atrial arrhythmias in a 12 month "off-drugs" follow-up in 86% of their cohort predominantly suffering from paroxysmal AF.[10] Schmidt et al. were the first reporting on a markedly (35%) reduction in operators` radiation exposure. They were able to confirm efficacy in terms of acceptable acute success rates (95%) and freedom from AF in 73% of the patients predominatly suffering from paroxysmal AF in a 239 (184-314) days follow-up.[33] This is well in line with results from Hlivák et al. in a prospective study on 100 patients suffering from paroxysmal AF reporting a success rate of 63% after a single and 86% after a mean of 1.2 procedures in a 15 month follow-up.[38] Rillig et al. were the first evaluating the impact of personal experience on procedural parameters and outcome and found a continuous and significant reduction in procedural and radiation time in the first 75 procedures without further improvements thereafter. Furthermore they revealed a trend to improved outcomes after the first 25 cases.[36] Three groups compared procedural parameters and outcome of conventional manual navigation and robotic navigation in terms of Sensei™. Studies comparing the Sensei™ with manual navigation in AF ablation are listed in table 1.[35,37,40] A common finding of these studies is a significant reduction of total fluoroscopy time by application of the Sensei™. This may be due to an increased positional stability of the ablation catheter leading to more infrequent confirmation of the position of the catheter by fluoroscopic imaging. However, this seems to be surprising and may be traced back to the limited trust in accuracy of positional data given by the 3D mapping systems used in all of these studies. Another probably better possible explanation may just be the other way round. The operator in remotely directed procedures directs the 3D mapping system himself and therefore is able to adjust views continuously to his personal requirements without further interaction with another person taking care for the 3D. This is very likely to reduce the need of fluoroscopic visualization of catheters during the ablation procedures. In addition to a reduction

Table 1: Studies Comparing the Sensei™ Robotic Navigation System with Manual Navigation in Atrial Fibrillation Ablation

	Di Biase et al. 2009 (34)	Kautzner et al.2009 (39)	Steven et al. 2010 (36)
Patients (n)	390	38	60
Assignment robotic/manual (n/n)	193 / 197	22 / 16	30 / 30
Paroxysmal atrial fibrillation (n/%)	262 / 67	38 / 100	30 / 100
Persistent atrial fibrillation (n/%)	110 / 28	0 / 0	30 / 100
Procedure time robotic/manual (minutes)	185±66 / 183±49.8 (p=n.s.)	207±29 / 250±62 (p=0.007)	156±44.4 / 134±12 (p=n.s.)
Fluoroscopy time robotic/manual (minutes)	48.9±24.6 / 58.4±20.1 (p<0.001)	15±5 / 27±9 (p<0.001)	9±3.4 / 22±6.5 (p < 0.001)
Ablation time robotic/manual (seconds)		1641±609 / 2188±865 (p<0.01)	
Follow-up total or robotic/manual (month)	14.1±1.3	5±1 / 9±3	6±3
Freedom from atrial tachyarrhythmias robotic/manual (%)	85 / 81 (p=n.s.)	91 / 85 (p=n.s.)	73 / 77 (p=n.s.)
Major adverse events robotic/manual (%)	1.6 / 1.0 (p=n.s.)	0 / 0	0 / 0

in total radiation exposure Steven et al. found a reduction of operators` radiation exposure by more than 60%.[37] This is conclusive due to the fact that distance to the source of radiation is increased in remote procedures and radiation exposure decreases with distance to the X-ray tube. Taking into consideration that radiation exposure increases the risk of fatal malignant diseases in patients undergoing AF ablation procedures[41] and likewise will be harmful for operators, reduction in radiation exposure in remotely directed procedures is an important finding. The smallest non-randomized comparative study also reports on a reduction of total procedure times.[40] However, this is not confirmed by the others and Steven et al. in fact saw a strong trend towards prolonged procedures in their prospectively randomized trial .[37] Kautzner et al. provide data on total ablation time finding a significant reduction in their Sensei™ procedures.[40] This may be explained by higher catheter stability as well as higher contact forces due to the feedback on forces given by the Intellisense™ technology embedded in the Sensei™. A recent study evaluating the attenuation of electrograms during ablation of paroxysmal AF is supporting this not only by a similar finding in terms of reduced total ablation time but also by demonstrating a greater signal attenuation.[42] While no complications occurred in the smaller comparative studies Di Biase et al. report on five major adverse events (one groin hematoma in each group, two pericardial effusions in the robotic and one pericardial effusion in the manual group) without statistical significance in distribution between the groups.[35] The rate of pericardial effusion in these studies is in line with data from large surveys.[43] However, the overall complication rate in the comparative studies is low probably due to the fact that very experienced centers were involved in the procedures. Finally none of the studies found a significant reduction in AF recurrences after ablation by application of robotic navigation in terms of Sensei™. Three prospective trials are currently recruiting patients in a prospectively randomized fashion. The "Man and Machine Trial" is focused on freedom from AF in a 12 month follow up in patients with paroxysmal or short lasting persistent AF and is designed as a noninferiority trial. Secondary endpoints include fluoroscopy exposure, procedure time and dose for patients and operators, complications and esophageal injury as assessed by endoscopy.[44] Another trial initiated in 2008 including patients suffering from all types of AF[45] is focused on early PV reconnection as a primary endpoint and will also look for complication rates, costs, fluoroscopy times, radiation exposure, and long term success as secondary endpoints. A third study called ARTISAN AF conducted in the United States currently recruits patients for evaluation of absence of early onset of all serious adverse events, freedom from symptomatic AF from days 91-365 in terms of chronic procedural success and absence of esophageal injury or pulmonary vein stenosis through day 365 as primary endpoints in a prospective randomized fashion. Procedures in ARTISAN AF are conducted applying the NaviStar ThermoCool Catheter (Biosense Webster, Diamond Bar, CA). Secondary endpoints are acute success and late severe adverse events.[46]

Amigo™ Remote Catheter System

A recently published initial non-randomized multicenter study was conducted by Kahn et al.The investigators found a very high efficacy to reach predefined right sided targets without any complications .[47] Clinical data on efficacy of ablation procedures performed with the system is lacking.

Magnetic Navigation Systems vs. Sensei™ robotic navigation system

Data comparing the two remote navigation techniques established for AF ablation is scarce. Data from the German Ablation Registry in 176 patients show reduced fluoroscopy times and procedure times when the Sensei™ is used without any difference in acute outcome and in procedural complications. It seems to be hard to draw a final conclusion from this data not reporting on chronic outcome and probably derived from procedures inhomogeneous in settings and performed by operators at different points of their individual learning curves. However, it is nicely shown that fluoroscopy time is short in both techniques (15 vs. 22 minutes) and acute success rates are acceptable (99 vs. 94%; p=n.s.). Furthermore, data from this registry reveals a relatively low percentage of AF ablation procedures done remotely and manual navigation is still the predominant technique in AF ablation.[48]

Conclusions:

Remote navigation techniques so far failed to demonstrate an improvement of acute and chronic procedural outcome in AF ablation procedures. On the other hand there is no doubt that remote procedures reduce patients` and in particular operators` radiation exposure. Recent developments in remote navigation of additional essential tools are promising. Several prospective studies are under way.

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