

THE AFIB REPORT

Your Premier Information Resource for Lone Atrial Fibrillation!

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This first issue of 2014 brings with it a major change for The AFIB Report with the retirement of Hans and Judi Larsen who, together, have worked with tireless dedication and with such good cheer on behalf of all afibbers looking for answers to this vexing condition. Our heartfelt thanks and deep appreciation go out to Hans and Judi for a job very well done, indeed!

Not skipping a beat, Hans reviews the first two interesting studies on magnesium's role in AFIB, and a study looking at the possibilities of using the new NOAC anticoagulants as a 'pill in the pocket' protocol.

I then pick up the baton with a summary of a timely population study out of the Netherlands confirming an association of low serum potassium with future development of AFIB, not surprising news to frequent readers of this newsletter. Followed by an interesting study confirming, once again, that low heart rate associated with high-level physical fitness is, itself, associated with increased risk of AFIB in otherwise healthy middle-aged men. Moderation in most things, including exercise seems to be the message here.

In the last half of this issue we review just a handful of highlights from the recently completed Boston AF Symposium 2014 that I attended, thankfully held this year in Orlando. With far too many interesting topics to report on, we'll narrow the focus to a few for this issue, including key insights from basic science, such as the possibilities of 'Relaxin', an endogenous human hormone that has potent anti-fibrotic effects that may prove an effective agent for reversal, even possible prevention, of AFIB related fibrosis, if further research pans out.

A summary follows of two of the hottest topics this year, and from the past two years as well, with a look at developments in rotor research, as well as both invasive and non-invasive phase-mapping systems to detect said rotors and foci in the hopes of streamlining certain ablation protocols. We look, too, at the promising status of contact force (CF) catheter development from St. Jude Medical and Bio-Sense Webster, both of which are already in play in Europe, and with high hopes of US approval soon as well.

To wrap up, a short review of interesting news on the real world risks of catheter ablation, beyond the major centers and most experienced EPs, that underscores, once again, the wisdom of our long term emphasis here at The AFIB Report to choose your ablationist and center with care, discrimination and research for the best safety and peace of mind.

Finally, if you need to restock your supplements, please remember that by ordering through the on-line vitamin store you will be helping to defray the cost of maintaining the web site and bulletin board. You can find the store at <http://www.afibbers.org/vitamins.htm> - your continuing support is greatly appreciated.

Wishing you good health and lots of NSR,

Shannon

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Antiarrhythmic properties of magnesium recognized

HARTFORD, CT. Six years ago a group of cardiologists and pharmacologists at Hartford Hospital reported that afibbers are likely to be deficient in intracellular magnesium, and that a pre-procedure infusion of magnesium sulfate (4 grams providing 800 mg of elemental magnesium) may help prevent atrial fibrillation (AF) following cardiac surgery. They found no correlation between serum magnesium and intracellular magnesium concentrations, but noticed that the magnesium infusion and subsequent rise in intracellular magnesium level was accompanied by a 50% increase in intracellular potassium level.

More recent trials have confirmed that pre-procedure infusions of magnesium reduce the incidence of post-operative AF by 36 to 66% in the case of coronary artery bypass surgery, and by as much as 74% in patients undergoing aortic valve replacement. The optimum level of magnesium sulfate infused would appear to be about 8 grams (1600 mg elemental Mg) and infusing more than that actually reduces effectiveness. It is also clear that performing the infusions during or after the procedure is largely ineffective.

Intravenous magnesium prolongs the atrial refractory period (the rest period following a contraction of the heart muscle – AF cannot be initiated during this period) and shortens the QT interval (duration of the activation and recovery of the ventricular myocardium). A prolonged QT interval is associated with potentially life-threatening ventricular arrhythmias. Thus, co-administration of Mg when using QT interval-prolonging drugs like ibutilide (Corvert) and sotalol (Betapace) may be beneficial. An early study found that a magnesium infusion prior to or during an attempt to convert AF and atrial flutter (AFL) to normal sinus rhythm (NSR) using intravenous ibutilide increased the rate of success by 19% and decreased the need for electrical cardioversion by 34%.

The TIME (Treatment with Ibutilide and Magnesium Evaluation) study found that concurrent administration of magnesium increased the likelihood of successful chemical conversion of AF and typical AFL by 78 to 300% depending on Mg dose. Similarly, intravenous magnesium has been found to enhance (by a factor of 2) the ability of dofetilide (Tikosyn) to chemically convert AF and AFL.

A recent study concluded that a low serum level of magnesium is associated with an increased risk of developing AF. Analysis of data from the Framingham Offspring Study showed that participants in the lowest quartile of serum magnesium level (equal to or less than 1.77 mg/dL) had a 50% greater risk of developing AF during a 20-year follow-up than did those with a serum level at or above 1.99 mg/dL.

The Hartford researchers conclude that adequate magnesium status is important in preventing the development of AF – that magnesium infusions prior to chemical cardioversion substantially improves conversion rates, and that the incidence of AF following cardiac surgery can be significantly reduced by pre-operative Mg infusions.

Ganga, HV, et al. Magnesium adjunctive therapy in atrial arrhythmias. PACE, Vol. 36, October 2013, pp. 1308-18

Editor's comment: The importance of an adequate magnesium status has long been recognized by readers of The AFIB Report, and many have found substantial relief by supplementing with this hugely important electrolyte. It is gratifying to see that the medical profession is moving towards incorporating magnesium into their armamentarium of agents designed to aid in the prevention and management of

atrial fibrillation and atrial flutter. For more on the importance of magnesium see: www.afibbers.org/resources/PCmagnesium.pdf
www.afibbers.org/resources/magnesiumabsorption.pdf ... Hans Larsen

Pill-in-the-pocket anticoagulation

BOSTON, MA. Whether or not an atrial fibrillation (AF) patient is prescribed an anticoagulant depends largely on their stroke risk as expressed via the CHADS₂ or CHA₂DS₂-VASc score. For more on these scores see www.afibbers.com/atrial_fibrillation/stroke_risk_factors/M108d.htm. One or more points on either of these scoring systems calls for systemic anticoagulation with warfarin, or one of the newer oral anticoagulants. US guidelines still list aspirin as an acceptable alternative for low- or moderate-risk patients; however, European guidelines no longer do so due to the by now overwhelming evidence that aspirin does not protect against cardioembolic stroke (stroke caused by a blood clot originating from the left atrial appendage or left atrium wall).

It is generally accepted that it takes about 48 hours for a clot to form as a result of AF. However, there is now evidence that clot formation may be substantially quicker in the case of high risk scores and longer duration episodes. Studies have shown that clots may form after only 5.5 hours (measured from the onset of the episode) in patients with a CHADS₂ score of 2.

The ASSERT study (asymptomatic AF in patients with dual-chamber pacemaker) found that the average annual stroke risk was 4.9% in patients with episodes lasting more than 18 hours, but less than 1.3% in those with shorter episodes. Another study involving 568 AF patients with implanted dual-chamber pacemakers found that in those with CHADS₂ scores of zero or above 2, duration of AF had little effect on stroke risk. AF burden was, however, very useful in risk-stratifying patients with CHADS₂ scores of 1 or 2.

Essentially, the authors conclude that stroke risk is elevated in patients with a high CHADS₂ score even if their AF burden is low and in patients with a low CHADS₂ score if their AF burden is high. They conclude that, "among patients with low to intermediate CHADS₂ scores and low burdens of AF, the risk of thromboembolism may be low enough to stop anticoagulation." Several studies are now underway to determine the relationship between AF burden and stroke risk using implantable pacemakers, ICDs or notably, the new Medtronic REVEAL XT cardiac monitor, which is lead-less and implanted subcutaneously.

While it makes intuitive sense that longer episodes would increase stroke risk, there is still doubt as to the real importance of AF as a stroke risk factor. In the 2009 TRENDS study, of 40 patients with stroke (cerebrovascular event or systemic emboli), 50% had no atrial tachycardia or AF detected prior to the event, and another 23% had no atrial arrhythmia detected in the 30 days leading up to the stroke. In a separate study of 560 heart failure patients, over a third of those suffering a thromboembolic event had no prior atrial high-rate episodes recorded. Furthermore, it was not at all clear whether the observed strokes were actually cardioembolic in nature. The authors draw the following conclusion.

"While it is obvious that not all strokes in an AF population are cardioembolic in nature, it remains unknown whether rapid anticoagulation soon after the onset of an AF episode can prevent thrombus formation and thromboembolic events even in the future when sinus rhythm has been restored."

Zimetbaum, P, et al. *The importance of atrial fibrillation burden and the origin of device-tailored anticoagulation.* PACE, Vol. 36, November 2013, pp. 1319-24

Editor's comment: The idea of prescribing anticoagulation depending on risk score and afib burden is an intriguing one indeed and could possibly lead to a pill-in-the-pocket approach using one of the new, quick-acting, oral anticoagulants. However, the finding that over 70% of thromboembolic events, stroke included, are not associated with a previous AF episode within the last 30 days casts some doubt on the utility of this approach. The finding does, however, support my long-held belief that AF, on its own, is a relatively minor factor in predicting stroke risk. The comorbid conditions most often accompanying AF

such as heart disease, hypertension and diabetes are, in my opinion, far more important. For example, the presence of hypertension doubles stroke risk, and diabetes is associated with a 2- to 5-fold increase in stroke risk even in the absence of AF... *Hans Larsen*

Serum potassium level and risk of atrial fibrillation: The Rotterdam study

ROTTERDAM, NETHERLANDS. As noted in the previous review on intracellular magnesium and its importance in preventing AFIB, there have been a good number of studies in recent years confirming the supportive relationship of magnesium and AFIB. In contrast, fewer studies to-date have looked at the association between serum potassium and AFIB, and less still via a large population-based study as reported below from Rotterdam, the Netherlands.

The study population comprised 4,059 community-dwelling elderly Dutch people with a mean age of 69.2 years and all initially without AFIB, who were tested at the outset for baseline serum potassium levels and followed for a mean period of 11.8 years (SD = 5.2yrs), then assessed for the development of AFIB and other cardiovascular conditions. During this time span, 474 participants developed atrial fibrillation.

Participants with hypokalemia (<3.5mmol/L) had a higher risk of AFIB (HR: 1.63, 95%CI: 1.03 – 2.56) than those with normokalemia (3.5 – 5.0mmol/L). And this association was independent of age, sex, serum magnesium and other potential confounders. The association between hypokalemia and myocardial infarction was especially pronounced as this group had an even higher risk of developing the arrhythmia during the long study period.

The rather straight-forward conclusion from the data is that low serum potassium levels are associated with a higher risk of AFIB ... which will come as no surprise to long-time readers of *The AFIB Report*.

What is interesting, and makes both intuitive sense as well as being understood by many readers of this newsletter who have followed their own AFIB/potassium association, is the finding of a progressive increase in AFIB risk with a progressive drop in serum potassium level. The mean serum potassium level measured at the outset was 4.10mmol/L (SD=0.31) and ranged from 2.40 – 5.51mmol/l. Many affibbers here have anecdotally reported a progressively less stable rhythm below 4.0mmol/L serum potassium.

When measured in quintiles, the lowest quintile of serum potassium level was associated with the highest risk of AFIB, and higher than the median (reference) quintile. In addition, this association remained statistically significant in a multivariable adjusted model (HR: 1.62, 95%-CI: 1.02-2.55)

The study also found that low serum potassium is associated with an increase in P-wave duration which is a marker of atrial conduction time. P-wave duration increase was associated as well with higher risk of AFIB in another study of hemodialysis patients.

The authors of the study propose that the most likely mechanism through which low serum potassium leads to increased risk of AFIB is via the influence of potassium on cell membrane potential. They propose that low serum K causes cellular hyper-polarity, increases resting potential and hastens depolarization. They note as well that no causality can be affirmed from these results and it cannot be excluded that low potassium level might be a marker for underlying conditions which predispose to AFIB.

Krijthe BP, et al, Serum potassium levels and the risk of atrial fibrillation, Int. J. Cardio Vol168, Issue 6, October 2013, pp. 5411-5415

Editor's comment: Hyper-aldosteronism comes to mind as one such potential underlying condition that may result in both low serum potassium and an increased risk for AFIB. However, it is highly doubtful

that excessive aldosterone production is the sole driver behind all associations of low serum potassium with higher AFIB risk. In this issue, we see fresh support implied for the strategy recommended to our readers for over a decade, of insuring adequate IC magnesium and potassium stores as a potentially sensible AFIB mitigating measure. Keep in mind, that while there is poor correlation between IC and serum magnesium, there is closer correlation between IC and serum potassium. The take home message is that both low IC magnesium and low serum potassium are associated with increased AFIB risk, giving further credence to insuring repletion of these vital electrolytes when found to be low as an adjunct to other measures used to treat atrial fibrillation ... *Shannon Dickson*

Low heart rate predicts incident AFIB in healthy middle-aged men

This interesting study is based on the previous association noted between low resting heart rate (HR) and AFIB in athletes. The aim here was to study whether low HR at rest or during exercise testing was a predictor of AFIB in initially healthy middle-aged men.

A total of 2014 Norwegian men were recruited for this prospective cardiovascular survey which comprised standardized bicycle exercise tests from 1972 – 1975. Over the course of 35 years or less of follow-up (53,000 person years of observation), 270 men (13%) developed AFIB. Low exercise HR was established after 6 minutes at the moderate workload of 100W (HR100W) and was found to be a significant long-term predictor of incident AFIB.

Men with HR100W <100bpm (n=260) had a high degree of physical fitness, low resting and low maximum HR, and a 1.60-fold increased AFIB risk (95% CI, 1.11-2.26) compared with men with HR100W equal to or above 100bpm when adjusted for age, systolic BP and physical fitness. Additional adjustments for relative heart volume slightly reduced the association. A subgroup of men in this cohort (n=860) with hypertensive BP measured at baseline had the highest risk difference between low and high HR100W with a hazard ratio 2.08 (1.19-3.45).

Of interest, of the 2014 initially healthy middle-aged men, 13% developed AFIB. A low HR after 6 minutes of exercise at 100W workload was not only a significant predictor of AFIB, but this same subgroup of men with low HR100W comprised a predominately low-risk group for overall CVD with low BP and high physical fitness.

Several prior studies have shown that high resting HR is associated with increased morbidity and mortality, while low resting HR is generally associated with better fitness and good prognosis. Nevertheless, this study also confirms earlier associations between low resting HR, high fitness and yet demonstrate a trend toward increased AFIB risk among fit men with low HR at rest. As such, there appears to be a U-shaped curve relating AFIB to resting HR. In addition to the association of increased AFIB with low resting HR, a small portion of men with resting HR at or above 85bpm also showed increased crude event rates of AFIB.

Furthermore, an increase in heart stroke volume, which is common over time with related endurance exercise and low HR, is also associated with increased AFIB risk, implying that it may be the increase in left atrium volume that could account, at least in part, for the elevated AFIB risk in this cohort of study participants. Furthermore, the finding that a combination of elevated stroke volume, low HR and elevated baseline BP was associated too with considerably increased AFIB risk, might also be explained by an imbalance in the autonomic nervous system (ANS), such as between sympathetic and vagal influences ... a potential connection familiar, once again, to long-time readers of *The AFIB Report*.

In conclusion, low HR at moderate exercise, associated with a high degree of fitness and elevated heart volume, seems to predict AFIB in middle-aged men, possibly due to a relative predominance of parasympathetic (vagal) activity, while baseline elevated BP significantly amplifies the risk. Interestingly, the predictive impact of high BP was stronger with concomitant low HR.

Grundvold, et al, Low Heart Rates Predict Incident AFIB in Healthy Middle-Aged Men, Circulation Arrhythmia & Electrophysiology, 2013; 6: 726-731

Editor's comment: The conclusion that low HR at moderate exercise associated with high fitness levels and elevated heart volumes may be due to a relative predominance of parasympathetic activity is only one possibility. A companion letter published by *Morris et al*, in the same issue of ***Circ Arrhyth & EP***, highlights recent findings that point to an alternative explanation for the observed association. Sino-atrial node electrical remodeling is associated as well with HR adaptation to exercise and a similar form of remodeling has been seen with sinus node dysfunction connected with aging and heart failure and frequently coexists with AFIB. Structural remodeling due to low voltage scar and fibrosis may thus also play a role in the amplified risk of AFIB associated with low HR in otherwise fit middle-aged men. Furthermore, models of endurance exercise have shown increased collagen deposition and fibrosis in both atria. As such, the potential role of electric remodeling and atrial fibrosis should also be explored, along with the possible link to autonomic tone, as a contributor to the pathophysiology of exercise-induced AFIB ... *Shannon Dickson*

Highlights from Boston AF Symposium 2014 – Orlando, FL

The 2014 Boston AF Symposium, mercifully held this year in Orlando during the 'polar express' deep freeze throughout the northern parts of the US, was the antithesis of cold and lethargy. On the contrary, the packed three day program attended by an army of EPs from around the world was charged with a notable air of excitement and focus about what was more than once labeled during the symposium 'this golden age' of electrophysiology that we are living through, with such rapidly advancing knowledge and practical clinical progress about atrial fibrillation.

In the remainder of this issue of *The AFIB Report*, we'll take a summary look at only a handful of highlights presented by a collection of international leading lights in this truly dynamic and evolving field of AFIB research and clinical progress.

Basic science research – towards a deeper understanding

Dr. Stanley Nattel from the Montreal Heart Institute got the initial day's sessions started by looking into new insights into *Mechanisms Underlying Focal Atrial Ectopic Firing*.

Dr. Nattel's talk included a review of several fascinating areas of on-going basic research, discussing such things as the relationship of a mutation in the protein Junctophilin-2 (JPH2) which interferes with the stabilization of the Ryanodine Receptor (RyR) located within heart cells causing a RyR dysfunction leading, in turn, to excessive leaks of Calcium ions (CA²⁺). Thus, resulting in too high an increase of CA²⁺ in the cell which can lead to sustained ectopic action that may well trigger AFIB ... a relationship that most readers of *The AFIB Report* are aware of from our frequent discussions of the risks of excess cellular calcium expression in potentially destabilizing heart rhythm.

Others, including Dr. Jose Jalife from University of Michigan, underscored the relationship between the two predominant types of AFIB, paroxysmal (PAF) and persistent AF (PeAF), with electrical and structural remodeling respectively. In other words, electrical remodeling prevalent in PAF is characterized by ion channel expression changes, while structural remodeling is characterized by fibrosis and substrate modifications common in persistent and permanent AFIB.

Dr. Jalife noted that differential changes in Sodium ion, Calcium ion and Potassium ion channel expression may thus explain the shift from paroxysmal toward persistent AFIB. As such, it appears that L-type calcium channel expression remodeling is faster in earlier stages of paroxysmal AFIB and slows down during the later transition from PAF to persistent AFIB. When persistent AFIB starts to stabilize, by that point, L-type calcium channel remodeling is complete and stable as well. From there on, expression of PeAF is characterized by structural remodeling with subsequent substrate fibrosis rather than by electrical remodeling as in PAF.

Relaxin-Serelaxin hormone: a new pharmacological approach for fibrosis reversal and AF prevention?

One of the more intriguing revelations by Dr. Nattel concerns promising early work with the universal mammalian hormone 'Relaxin' ... a powerful endogenous anti-fibrotic hormone. *Relaxin* is best known for its role in relaxing the uterus during pregnancy, but also turns out to have some cardio-protective benefits, in addition to potentially treating pain in fibromyalgia-like syndromes.

He discussed two recent studies, the first by: *Parikh A, et al, Relaxin suppresses AFIB by Reversing Fibrosis and Myocyte Hypertrophy and Increasing Conduction Velocity and Sodium Current in Spontaneously Hypertensive Rat Hearts (SHR). (Circ Res. 2013;113: 313-321).*

This study demonstrated that *Relaxin* treatment suppressed AFIB in hypertensive rats and provided compelling evidence that *Relaxin* may prove to be a novel therapy to manage AFIB in humans by reversing fibrosis and hypertrophy as well as by modulating cardiac ionic currents.

A second study looked at the *Relaxin* derivative 'Serelaxin' (recombinant human relaxin-2) in acute heart failure showing a potential benefit in CHF treatment and management. *Serelaxin*, which has already shown some benefit *in vivo* in humans, could potentially be made into an oral drug for AFIB treatment. It showed a reduction in 180 day mortality with fewer signs of organ damage and more rapid relief of congestion during the first days after administration in a pair of double-blind, placebo-controlled trials: *M. Metra, et al, Effect of Serelaxin on Cardiac, Renal and Hepatic Biomarkers in the Relaxin in Acute Heart Failure (RELAX-AHF) Development Program: Correlation with Outcomes. J Am Coll Cardiol. 2013, Jan 15;61(2):196-206.*

On a personal note, an internationally renowned endocrinologist and hormone expert from Brussels, Belgium recommended in 2010 that I consider adding *Relaxin* to my own treatment regime as a possible aid for a chronic pain condition relative to my childhood bout with polio in 1962. Alas, it is not yet sold in the US, and thus it may still be some time before it's available in US pharmacies.

This physician noted at the time that in addition to helping with a fibrotic pain condition, it potentially might also benefit my AFIB issue longer term due to its powerful anti-fibrotic effect. Apparently, he was ahead of his time on this issue, as he has often been before in his own field. Not surprisingly, it certainly grabbed my attention when Dr. Nattel first shared these recent studies with *Relaxin* as a possible direct means to reverse, and possibly even prevent, AFIB related fibrosis in humans from structural remodeling.

Mind you, this is all still quite preliminary and not yet fully vetted by any means, but does appear promising and bares close attention in the coming years. It would be outstanding if this endogenous human hormone found in both men and women, used as an exogenous therapeutic agent, proves itself a viable front line preventative treatment for AFIB. Fortunately, *Relaxin* also appears to be remarkably safe in normal physiologic doses.

Like many hormones, its production tends to decline with age ... perhaps it's not so surprising then that we see the majority of AFIB kicking in during middle age and older when the milieu of hormonal and other biochemical changes associated with aging start to set in, including perhaps functional declines in what may well be a potent endogenous anti-fibrotic hormone. Further work should help clarify the role of *Relaxin*, and its recombinant analog Serelaxin, not only as a potential AFIB therapy, but possibly for prophylaxis as well. Not to mention its possible role in other fibrotic conditions.

Tranilast anti-fibrotic TGF- β inhibitor and Galactin-3 inhibitor progress

Dr. Nattel and others also reviewed his work investigating the role of *transforming growth factor-beta* (TGF- β), a protein that evidence suggests may encourage AFIB substrate remodeling, and a molecule called *Tranilast*, a TGF- β inhibitor with the potential to also help prevent fibrosis as another promising agent with a different pharmacological pathway than *Relaxin*, but with a similar goal.

Finally, more work is progressing on a Galactin-3 inhibitor and its potential as a drug to prevent AFIB from ever taking hold, if used very early after the initial stage of the condition manifests. Clinical trials are underway.

Rotors, ECGI and phase-mapping: moving towards a better understanding

A hot topic in Orlando on-going from the past couple of years in Boston, was the evolving research into rotors and foci captured via phase-mapping or ECGI (electrocardiographic imaging), both invasive as in the Topera system championed by Sanjiv Narayan and the FIRM ablation concept, and by several non-invasive systems including the Cardio-Insight body surface scan phase-mapping vest, as well as a closely comparable phase-mapping vest system evaluated by Karl Heinz-Kuck in Germany.

Both of these non-invasive phase-mapping vest systems employ 252 to 256 sensors, respectively, across the front and back of the torso for creating a global spatio-temporal phase map via analysis of body surface potentials from each heart beat to help better identify rotors, or re-entrant drivers, as possible ablation targets across both atriums.

Dr. Jalife describes rotors as center points or singularities where all the phases of a given action potential converge to a single three-dimensional center point. Each phase of an action potential is color-coded with the wave-fronts of each phase, as well as the rear part or 'tail' of a given phase, both meeting at that center point or singularity.

When viewed from each end of a given rotor, you would see expanding spinning 3D wave-fronts either from the endocardial view or the epicardial viewpoint. A rotor originating from its singularity will extend throughout the full thickness of the atrial wall and is represented graphically as a colorful spiral wave with a rotor-like pattern. In practice, these 'rotors' look very much like spinning multi-hued pin-wheels ranging from roughly 2mm to 4mm diameter where the wave-front starts very slowly at the center and expands out with increasing velocity the further the wave propagates away from the singularity.

Conceptually, a rotor can be thought of as organizing centers for AFIB where all phases representing action potentials converge.

What is the clinical significance of rotor identification via phase-mapping?

The clinical potential, if this technology pans out as their developers and promoters project, is potentially shorter, more targeted and more effective ablation protocols for both paroxysmal and particularly persistent AFIB ablations. That is the ideal; however, there are still several big challenges in interpreting rotor function, and discerning their possible role in a given arrhythmia as well as determining which rotors or foci are key ablation targets and what approach one should take in trying to ablate a given rotor.

In addition, it is not yet clear how much these new mapping systems and their focus on rotors will really buy us when compared to the solid results now achieved from highly sophisticated activation maps using current state of the art tools like 3D electro-anatomical mapping, ICE (intracardiac echocardiograph) and both combined with the skill of a top ablationist?

Firstly, many of these rotors are unstable, meandering and transitory, some lasting no longer than half a cycle length. In addition, some of these rotors tend to drift across the atrium and bounce off of physical

barriers such as scar tissue, a valve orifice, ridges, etc. making selection of an ablation candidate more challenging. What looks like a stable rotor via one phase mapping system may look like an unstable rotor in another higher resolution mapping system, possibly further muddying the waters at this stage.

The idea, at this point in the still gestational understanding of this area of mapping research, is to identify those rotors associated with the highest dominant frequency in a given area as a key target zone in hopes of being able to perform a more tailored ablation with a potentially shorter procedure time and with more confidence in the result, especially with less experienced operators now venturing beyond the PVs, yet potentially might be of help even to the most experienced EPs as well.

Professor Haissaguerre and his team in Bordeaux are deeply involved in developing practical clinical strategies based on rotor identification. They combine pre-ablation CT scans and body surface scans via phase-mapping and integrating them with 3-dimensional electro-anatomical mapping data (Carto-3D or Ensite NavX) obtained during the ablation to determine the optimum ablation strategy.

Nevertheless, it's clear at this stage that more research into validating these ECGI phase-mapping systems with accurate EP voltage data using real-time 3D anatomical mapping inside the heart, as well as confirming the preliminary shorter term results over longer periods of time such as over a 1.5 to 2 years plus window, is a key step needed toward better defining and confirming for certain if these new mapping technologies stand up to the test of time and deeper scrutiny.

Haissaguerre also noted that, practically-speaking, it's generally more accurate to describe these rotors detected by Cardio-Insight's *ecVUE* phase-mapping vest as congregating in '*arrhythmogenic regions*', rather than to think of them as stable rotor points or specific focal points to target. In other words, what the *ecVUE* vest provides is a pre-ablation view of regional re-entry driver activation in the form of rotors mostly which are most commonly found in already well-known arrhythmogenic regions of the left and right atriums.

Not surprisingly then, Haissaguerre also confirmed that the top three regions where these 'rotors' tend to congregate are around the pulmonary veins and antrum area, the posterior wall of the LA and the left atrial appendage (LAA).

Several members of the Bordeaux group have made substantial ownership investments in Cardio-Insight as testimony to their interest in the technology, and they report preliminary results claiming roughly a 50% reduction in the number of non-PV ablation lesions required for either AF termination or for conversion to tachycardia, compared to their traditional 'step-wise' ablation strategy used for persistent AFIB cases.

While these very early results look promising, similar hopeful findings helped launch the CAFÉ approach some years ago, only to fall more or less by the way side when other centers could not replicate nearly the degree of success of the early promoters. More than one EP remarked in Orlando about the apparent similarities of the phase-mapping/rotor push going on now to that of the initial CAFÉ excitement. Nevertheless, it's certainly intriguing and worth finding out what its ultimate merit may be.

Dr. Karl Heinz-Kuck, renowned German EP and researcher, is a proponent of investigating this new phase-mapping technology and has worked extensively with an alternative 256 sensor vest-based system that is very similar to Cardio-Insights *ecVUE*. After the last few years of work with this new technology, he is cautiously optimistic in the future possibilities and potential application of phase mapping. However, in the same breath, he also cautions that it is not yet ready for widespread adoption by EP labs around the world doing front-line ablations.

Heinz-Kuck noted that often times, and to his surprise, when he ablates either the center of many stable rotors, or draws an ablation line through them, there was no change at all in the AFIB as a result! He also emphasized the potential risks, noting that ablating certain stable rotors could perhaps even further stabilize or fix the rotor, the opposite of what you would want. Dr. Jalife also implied this possibility when he, too, cautioned that there was still much to learn before he can comfortably recommend wide-scale

adoption of ablations based on interpretation of rotors derived from our still-evolving understanding of the process.

That being said, Dr. Jalife is confident that the insights gained from his and others research so far do indeed confirm now that rotors play a significant role in the mechanism of AFIB, and that further research, now on-going in his and other labs around the world, will surely help better define what role that knowledge might play in guiding future ablation strategies, and possibly other treatment modalities for AFIB.

Bottom-line, stay tuned to this topic, but don't postpone a needed ablation and risk further substrate remodeling in hopes a major breakthrough is just around the corner any time soon. The top-tier operators in the world already achieve very good results even in difficult persistent cases, and whenever any of these new mapping methods, as well as other new ablation tools, are proven to significantly add benefit to the best of current day cutting-edge technologies and strategies, you can be sure that the most experienced top EPs will quickly adopt the latest 'proven' technologies as well into their own protocols. Choose the best EP you can find and then trust their technology choices on your behalf.

Contact Force catheters: leading toward more consistent ablation results

One of the more anticipated near term developments in ablation technology that is currently in use in European trials and for which FDA US approval is anticipated in the not too distant future, is the advent of Contact Force (CF) catheter systems. These new catheter systems were not only featured by Dr. Mousa Mansour during his presentation on the subject during the symposium in Orlando, but were also clearly explained and featured by Drs. Andrea Natale, Dhanunjaya Lakkiready and Gerhard Hindricks during an evening industry presentation over dinner.

St Jude Medical presents with the Tacti-Cath CF catheter technology, the patent for which was acquired in August 2013 with St Jude's purchase of Endosense. Tacti-Cath uses a novel fiber-optic force-sensing method and has a number of desirable features. The other big player in CF catheters is Biosense Webster with their new Smart-Touch CF design based on their own industry leading latest Thermo-cool irrigated catheter, with the added bonus of a spring-loaded CF-sensing RF ablation catheter tip. The Smart-Touch also integrates fully with 3D EAM mapping systems in real-time, such as their own popular Carto-3D EAM system.

Dr. Mansour emphasized that with the ability to provide real-time force-sensing feedback to the operator for the first time, they could better gauge the precise amount of force that is applied at the critical tip-to-tissue contact. As such, there is real hope that operators of all skill levels will have a valuable new feedback tool to know just how much contact force, time and power/temp is being applied at each lesion, leading to more consistent trans-mural lesion creation and, hopefully, less repeat ablations needed due to reconnected PVs and other non-PV ablation sites. Understandably, this development is eagerly awaiting approval and further study to confirm its anticipated utility.

Ablation safety: the good news and the caveats

We all know that endocardial catheter ablation for AFIB is a reasonably safe invasive procedure, right? With a high margin of good outcomes and a very small degree of procedural risk, though there are some real risks to be sure. Well, it seems the answer is a qualified 'yes' ... it is impressively safe ... at least in the right hands, at better centers.

The majority of risk data to-date, most of which was done at large high volume ablation centers employing highly-skilled ablationists, emphasized the very positive results we've all come to trust. That is, until a recent long ten year survey by *A. Deshmukh, et al, 'In-Hospital Complications Associated with Catheter Ablation of Atrial Fibrillation in the US between 2000 -2010. **Circulation, 2013;128:2104-2112.***

This study of 80,000 ablations, assessed center/operator volume and skill associated with adverse complications and focused on the average scenario beyond just the high volume centers and most experienced EPs. Interestingly, 80% of all ablations were performed at low volume smaller hospitals doing around 50 ablations a year with EPs averaging around 25 AFIB procedures a year. Little wonder then that in this larger cohort of lesser experience operators there were an increasing number of complications over that ten year period. It is not that less skilled ablationists were getting worse at their craft over time, but rather this finding reflects that more EPs were doing ablations with less than top-tier training and experience.

Surprisingly, this study from 2000 through 2010, found that 1 out of every 243 patients did not make it out of the hospital after their ablation! Not such great news, indeed, for those on the wrong side of that number. Keep in mind, that the take home message here ... and one that *The AFIB Report* and *afibbers.org* bulletin board have emphasized repeatedly over the last 13 years ... is that the most important decision a prospective AFIB ablation patient has to make is choosing the most experienced and highly-skilled ablation EP they can arrange for themselves.

There are many excellent and remarkably safe AFIB ablation operators, and a constantly growing number all the time, who are available at numerous ablation centers across the US and Europe. Just make sure you do your homework and don't skimp on this one decision you want to get right. The more experienced and better skilled EPs maintain a stellar track record for success with very low adverse events. Choose from among the growing number of high quality EPs at centers with solid reputations and be at ease with your decision. Don't be afraid, be smart instead and do your homework (that is what we are all here to help with after all) and your odds for a great outcome well be very high.

Procrastination has a price

We all know the drill when it comes to considering either an ablation, or more conservative treatment options, for a relentlessly progressive AFIB burden over time. We at *The AFIB Report* encourage and try to provide a well-rounded education about all of your options, including pharmaceuticals when appropriate, while emphasizing from the beginning the value of supportive nutritional and dietary protocols as well as life-style modifications that can very much contribute to a more stable heart and better overall health as well.

However, a growing wave of research in recent years, reinforced by anecdotal experience as well, indicates that one should think twice and not procrastinate too long in the face of on-going progression of AFIB episodes that are not responsive enough to whatever combined management protocols we have adopted. Doing everything one can to quiet the heart is always good, but using that approach as an excuse to avoid an expert ablation when your AFIB is still much too active and symptomatic, and in spite of heroic efforts to control episodes, will only make a future ablation less likely to be successful. It can be a fine line choice, but the current evidence reinforces the wisdom of knowing when not to wait longer to add in such an expert ablation as the cornerstone for buying as much NSR time in your life as possible. Not procrastinating too long is particularly important for those who recently converted to persistent AFIB.

Those who are able to gain full control over active AFIB with either nutritional repletion of vital ionic minerals and nutrients, and/or a drug regime, for a long period of time, and can confirm the absence of silent AFIB episodes, then all power to you! But, if your conservative program is less than fully effective after six months to a year maximum of diligent effort and you are still being tormented by episodes of AFIB/Flutter, then by all means, don't put off finding the best ablationist you can arrange for yourself and confirm if, indeed, a skilled ablation is your next best step for long term peace of heart.

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