

# Heart Rhythm 2009 i Boston 13. – 16. mai

**Eivind Platou, Oslo universitetssykehus, Ullevål**

**F**orsommeren i Boston er en fin tid og passe varm, selv om havtåken kan komme og overraske med sjokkvkjøling. Vi merket godt finansbølgene med superutsal overalt, selv om det virket folksomt nok langs handlegatene. Boston er en fin by med europeisk preg og veldig mye historie.

Heart Rhythm er en stor kongress, i år med 13 000 deltagere fra 70 land. Det var den 30. kongressen (tidligere NASPE), som i starten var mest sentrert rundt pacemakere. Det var opptil 22 parallelle sesjoner. Hvis man ville, kunne man begynne kl. 8 om morgenen og fortsette til 6 om kvelden, før alle satellittsymposiene startet. Parallelt går det, som tidligere, et atrieflimmer-symposium, AF Summit, med egen påmelding. Første dagen er viet mini-kurs som er effektive kurs med egen påmelding og avgift.

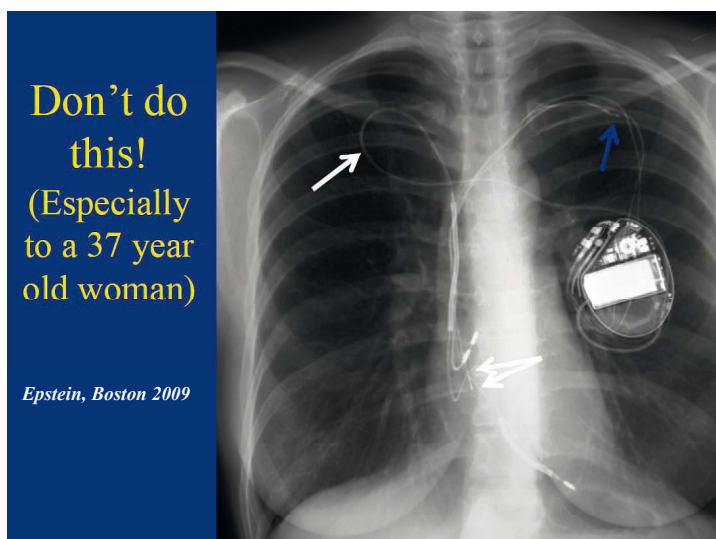
## Ekstraksjoner

Fra mitt ståsted var kongressen mye preget av fremleggelsen av nye retningslinjer for ekstraksjon. De kan lastes ned fra [www.hrsonline](http://www.hrsonline).

org og vil bli trykket i julinummeret av Heart Rhythm Journal. "Ekstraksjonsfolket" har i alle år jobbet for å få i alle fall ett symposium om ekstraksjoner, men det har vært tregt. Cleveland har som trøst i flere år arrangert kveldsmøte med dette temaet med Bruce Wilkoff som suveren leder av ekstraksjonsmiljøet. Dette møtet ble i år brukt til å fremlegge de nye retningslinjene. I tillegg var det ekstraksjonssymposier ved nesten alle sesjonene, til og med parallelt. De nye retningslinjene brakte ikke noen store overraskelser, i alle fall ikke for oss i "bransjen". Men de presiserte grundig kravene til ekstraksjonssentrene. Det

har vært rapportert alvorlige komplikasjoner og dødsfall i forbindelse med ekstraksjoner av Sprint Fidelis-elektroder (se under) gjort på sentra uten tilstrekkelig kompetanse og sikkerhet. For ICD-elektrodeekstraksjoner er normalt suksessraten 100 % uten mortalitet og under 1 % alvorlige komplikasjoner på kompetente sentra. Dette må være utgangspunktet for indikasjonstillingen. Komplikasjonsraten faller raskest i begynnelsen, men faller fortsatt forbi 400 pasienter (Ullevål har behandlet 450 pasienter).

Retningslinjene er helt klare på at ved infiserte anlegg skal hele anlegget fjernes (klasse IB), det skal ikke forsøkes med revisjoner, selv om det tilsynelatende bare er infeksjon lokalisert til lommen. Litt nytt er IB-anbefalingen om at anleggene skal fjernes også ved valvulær endokarditt, selv om det ikke er definitiv involvering av elektroder eller device. Det samme gjelder gram positiv sepsis/bakteriemi. Persiste-



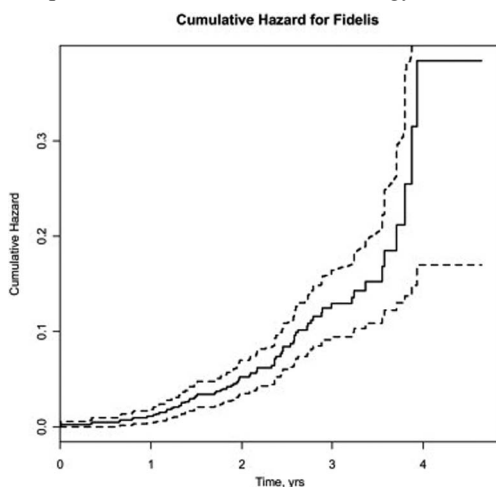
Figur 1 – selvforklarende?

rende okkult gram negativ bakteriemi er klasse IIB-indikasjon.

For funksjonelle og ikke funksjonelle elektroder er det klasse IC-indikasjon for fjerning av gamle ICD-elektroder. Det er IIA-indikasjon for fjerning av fungerende eller ikkefungerende elektrode for å få tilgang for å plassere en ny elektrode, og IIB-indikasjon for å fjerne overtallige elektroder "hvis det ikke er kontraindikasjon". Dette ble understreket av Epstein med et megetsigende thoraxbilde (figur 1).

## Sprint Fidelis

Sprint Fidelis-elektrodene ble gjenstand for mye diskusjon. Det var mange abstrakter vedrørende disse elektrodene. Det spesielle ved dem er ikke bare at de er hyppig gjenstand for brudd, men ved brudd får pasienten et stort antall urettferdige sjokk (rekorden i Norge er 67 støt) før man får stoppet apparatet ved å legge på en magnet eller inaktivere den med programmerer. Hausers (Minneapolis Heart Institute) beregninger (figur 2) var skremmende. Hans analyser viser at hvis elektroden fungerer normalt etter 1 år, er forventet overlevelse det neste året 96,0 % (97,5, 94,5). Hvis elektroden fungerer normalt etter 2 år, er forventet overlevelse det neste året 92,6 % (95,4, 89,8, og hvis elektroden fungerer normalt etter 3 år, er forventet overlevelse det neste året 77,5 % (95,8, 61,7). Elektrodene skiller seg veldig tydelig fra andre ICD-elektroder. Professor Epstein, Brigham and Woman's Hospital, Boston, fortalte at de var begynt med



Figur 2. Kumulativ risiko for svikt av Sprint Fidelis defibrillatorelektroder (heltrukken linje)  $\pm$  95 % konfidensintervall (fra R. G. Hauser).

profylaktisk ekstraksjon av Sprint Fidelis-elektrodene på yngre, aktive med pacebehov eller ICD-indikasjon sekundærprevensjon. Wilkoff var litt mer tilbakeholden, men var enig i en klasse IIB-anbefaling, mens andre mente det i dag var en klar klasse IIA-indikasjon. Det bør i alle fall vurderes ved generatorbytte og ved andre intervensjoner. Utviklingen er ubehagelig spennende, ettersom det er så mange elektroder av denne typen, 500 bare i Norge!

## Late breaking trials

Det var begrenset med spenningsmomenter, men spennende er resultatene fra de nye amiodarononderivatene. Dette er bredspektrede antiarytmika med effekter i nærheten av amiodaron, uten bivirkningene. Dronedaron nærmer seg raskt frislipp på markedet, mens neste kandidat, budiodarone har litt igjen.

Stefan H. Hohnloser fra Frankfurt presenterte ATHENA studien, en fase III randomisert, kontrollert studie av dronedaron på eldre pasienter med moderat til høyrisiko paroksysmal eller persisterende atrieflimmer og hjertesvikt. Studien omfattet 4 500 pasienter, og viste en reduksjon på 24 % på hospitalisering av kardiovaskulær årsak og "all-cause" mortalitet. Effekten var sterkest for hospitalisering og død relatert til atrieflimmer.

Michael Ezekowitz, fra Lankenau Institute for Medical Research in Wynnewood, PA, la frem PASCAL, en dobbelt-blind, randomisert, kontrollert studie over trygghet og sikkerhet for budiodarone, en analog til amiodaron, hos paroksysmal AF-pasienter med tokammerpacemakere som har AF-dataloggingsmuligheter. 72 pasienter ble randomisert til placebo eller budiodarone i dosene 200 mg, 400 mg eller 600 mg to ganger daglig i 12 uker. Primært endepunkt var prosent forandring i AF "burden" fra utgangspunktet til 12 uker. Pasienter som ble inkludert i studien hadde en baseline AF "burden"  $>3$  %. Resultatene viste en dose-respons-effekt av budiodarone. 200 mg reduserte "burden" med 10 % (NS). 400 mg ga en signifikant 54 % reduksjon i "burden", og pasienter som fikk 600 mg hadde et signifikant fall på 75 %. Til sammenligning hadde pasientene i placebogruppen en 8 % økning i AF "burden".

## Norske abstracts presentert i Boston

### **[AB22-1] A Genome-Wide Association Study in Icelanders Identifies a Novel Sequence Variant on Chromosome 16 that Associates with Common Atrial Fibrillation**

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Introduction: Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in humans and a major cause of morbidity and mortality. We have previously, through a genome-wide association study, reported on sequence variants on chromosome 4q25 that confer risk of AF. The 4q25 locus has since been found to be significantly associated with ischemic stroke, with the strongest risk for cardioembolic stroke. In the attempt to discover additional variants that associate with AF, we have expanded our genome-wide association scan by increasing samples with a broad AF phenotype. Methods: After quality filtering, 304,226 SNPs were tested individually in a sample of 2,385 Icelandic patients with AF and/or atrial flutter (AF1) and 33,752 Icelandic population con-

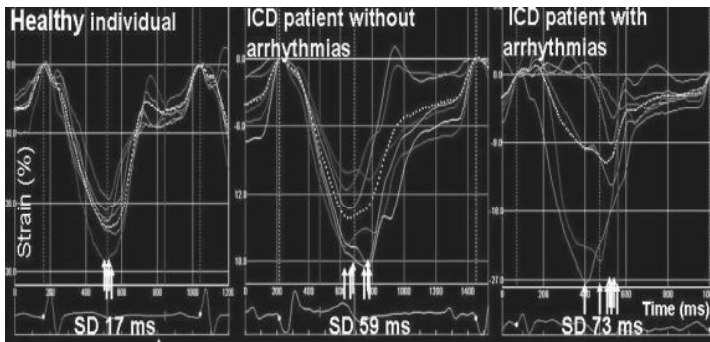
trols, genotyped with the Illumina HumanHap300 or HumanHapCNV370 bead chips. Of the top ten SNPs, seven represented the previously discovered signal on chromosome 4q25. The remaining three SNPs were genotyped in three replication sample sets of European descent, from Iceland (989 cases and 2,027 controls), Norway (725 cases and 725 controls) and the United States (735 cases and 729 controls). Results: One SNP, on chromosome 16, showed genome-wide significant association with AF in the combined Icelandic sample set and this association was replicated nominally in the non-Icelandic samples with constant direction of the effect. In the combined analysis of all four sample sets the odds ratio (OR) for this variant was 1.21 (95% CI: 1.14-1.29) with a corresponding P value of  $P=1.4 \cdot 10^{-10}$ . This variant does not associate with hypertension, coronary artery disease, or obesity, all known risk factors for AF. The population frequency of this sequence variant is 20% in the Icelandic control set. Conclusions: A sequence variant on chromosome 16 associates with common AF in populations of European descent. This is the second reported locus with a common sequence variant with association to AF that has been replicated in several populations and is further evidence of an important genetic contribution to the pathogenesis of this complex arrhythmia.

### **[PO02-107] Left Ventricular Mechanical Dispersion - A Novel Predictor of Ventricular Arrhythmias in Patients after Myocardial Infarction**

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Introduction: Electrical dispersion in the infarcted myocardium facilitates ventricular arrhythmia. Myocardial strain by echocardiography can quantify detailed regional myocardial function. We hypothesized that LV mechanical dispersion by strain echocardiography can predict risk for ventricular arrhythmias. Methods: We prospec-

tively included 30 post MI patients implanted with an ICD according to secondary prevention. After  $1.7 \pm 0.8$  years follow up, 17 had no and 13 patients had one or more arrhythmic events requiring ICD therapy. Healthy individuals served as control group ( $n=21$ ). Strain measurements were assessed by echocardiography. Standard deviation (SD) of time to maximum myocardial shortening in a 16 LV segment model was calculated as a parameter of mechanical dispersion. Results: EF did not discriminate ICD patients with arrhythmias from those without ( $38 \pm 8\%$  vs.  $40 \pm 13\%$ ,  $P=0.73$ ). Figure displays increased mechanical dispersion in an ICD patient with recorded arrhythmic events. (Arrows indicate timing of maximum shortening). ICD patients showed increased mechanical dispersion compared to healthy individuals ( $68 \pm 19\text{ms}$  vs.  $22 \pm 10\text{ms}$ ,  $P < 0.001$ ). Mechanical dispersion was significantly more pronounced in ICD patients with arrhythmia compared to those without ( $76 \pm 20\text{ms}$  vs.  $61 \pm 15\text{ms}$ ,  $P=0.03$ ). Conclusions: Mechanical dispersion assessed by strain echocardiography was present in post MI patients compared to healthy individuals. Increased mechanical dispersion predicted ventricular arrhythmias in post MI patients.



## [PO02-109] Wedensky Modulation Index Predicts Ventricular Arrhythmia Events In Patients with Prior Myocardial Infarction and Ejection Fraction less than 30% (MADIT II)

**Peter A. Brady, MD, FRCP, Paul Erne, MD, J. Val-Mejias, MD, Joerg O Schwab, MD, Rainer Schimpf, MD, Michael Orlov, MD, PhD, Tom Mattioni, MD, Marek Malik, MD, PhD, Jan Amlie, MD, PhD.. Mayo Clinic, Rochester, MN, United States; Kantonsspital, Luzern, Switzerland; Galichia Heart Hospital, Wichita, KS, United States; University of Bonn, Bonn, Germany; University of Mannheim, Mannheim, Germany; Caritas St Elizabeth's, Boston, MA, United States; Arizona Arrhythmia Consultants, Phoenix, AZ, United States; St George's Hospital, London, United Kingdom; Rikshospital, Oslo, Norway**

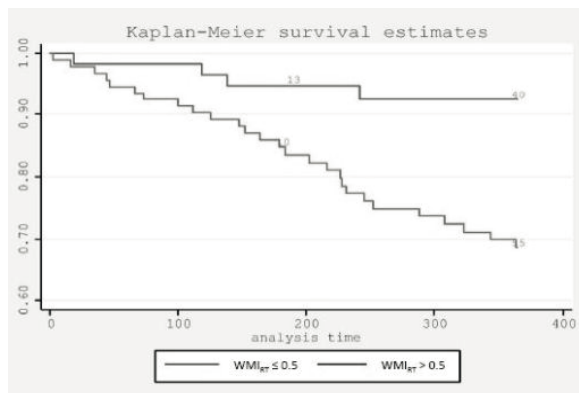
Introduction: Wedensky modulation (WM) testing

comprises subthreshold trans-thoracic electrical stimulation delivered to every other QRS complex. A WM index combining the analysis of the R-wave and T-wave (WMIRT), which has been shown to accurately predict ventricular arrhythmic (VA) events, was computed from electrocardiographic differences between stimulated and non-stimulated complexes.

We hypothesized that this index

might predict VA events in patients (Pts) with prior MI and a left ventricular ejection fraction of  $\leq 0.30$  (MADIT II). Methods: The WMIRT index was evaluated from a prospective observational study at 8 international centers. VA occurrences for MADIT II pts were compared to the WMIRT index. In total 149 pts with MADIT II criterion were studied: 57 with a negative index ( $\text{WMIRT} \leq 0.5$ ) and 92 with a positive index ( $\text{WMIRT} > 0.5$ ). Results: When the frequency of VA events was compared in Pts with a negative versus a positive WMIRT index there was a strong positive correlation ( $p=0.0024$ ) between WMIRT index and VA events with a positive WMIRT index indicating a significantly greater likelihood of a VA event than

a negative WMIRT index. Cox Proportional-Hazards Regression analysis determined a hazard ratio of 4.41. Conclusions: WMIRT index is a useful non-invasive tool for predicting likelihood of VA events in Pts with prior myocardial infarction and ejection fraction  $\leq 30\%$ .



### [PO05-149] Long-term Right Ventricular Pacing Thresholds and Sensing in High Posterior Septal Versus Apical Lead Placement in Cardiac Resynchronization Therapy

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**Introduction:** Little is known about electrophysiological lead performances in right ventricular (RV) lead placement in the high posterior septal (S) position in cardiac resynchronization therapy (CRT-P or CRT-D). **Methods:** Pacing thresholds, sensing electrograms and lead impedances were measured prospectively in 304 patients (51 upgraded to CRT) treated with CRT-P or CRT-D from 1999 to 2008. All patients received different Medtronic pulse generators and leads. Pacing thresholds were measured at 0,5ms and 2,5V at 1,3,6,12,18 and 24 months follow-up in all patients. Only new lead implants in RV apical (A; n= 87) versus S (n= 166) were compared. **Results:** No significant differences were found between pacing thresholds or sensing function in CRT-P (n=196) and CRT-D (n=57) in the same RV lead location. Consecutive pacing thresholds at 0,5ms were  $0,62\pm 0,66V$ ,  $0,82\pm 0,73V$ ,  $0,89\pm 0,72V$ ,  $0,91\pm 1,27V$ ,  $0,93\pm 1,77V$ ,  $0,81\pm 0,62V$  and  $0,82\pm 0,72V$  in S, and  $0,62\pm 0,27V$ ,  $0,64\pm 0,43V$ ,

$0,80\pm 0,54V$ ,  $0,80\pm 0,40V$ ,  $0,83\pm 0,39V$ ,  $0,80\pm 0,36V$ ,  $0,79\pm 0,30V$  in A (p=ns). Long-term pacing thresholds at 2,5V were stable at  $0,09\pm 0,05ms$  in the S and  $0,07\pm 0,10ms$  in A (p=ns), and electrograms varied between  $9,8\pm 4,2mV$  to  $14,5\pm 6,7mV$  in S and  $10,7\pm 4,1mV$  to  $18,0\pm 5,5mV$  in A (p=ns). The impedances were stable in S  $573\pm 92$  ohm and in A  $860\pm 270$  ohm, in CRT-P (p<0,001), and in S  $483\pm 76$  ohm and in A  $637\pm 198$  ohm, in CRT-D (p<0,01). Coronary sinus (CS) lead (n=304) pacing thresholds were stable at 0,5ms and 2,5V,  $1,17\pm 0,90V$  and  $0,14\pm 0,16ms$  in unipolar leads (n=232) and  $0,96\pm 0,50V$  and  $0,10\pm 0,09ms$  in bipolar leads (n=72; p=ns). The CS lead electrograms were stable at  $10,0\pm 3,7mV$  to  $16,1\pm 6,1mV$ . The CS lead impedances were  $594\pm 169ohm$  in unipolar and  $680\pm 181ohm$  in bipolar (p<0,05). The atrial pacing lead (n=218) thresholds were stable at  $0,62\pm 0,34V$  and  $0,06\pm 0,05ms$ , electrograms at  $3,6\pm 2,2mV$  to  $5,7\pm 3,6mV$  and impedances  $619\pm 251$  ohm during follow-up. **Conclusions:** On long-term both CS and RV leads in S and A demonstrated very good and stable pacing thresholds and sensing electrograms. The only significant differences were lower impedances in S compared to A lead location.

### [PO05-105] High Wedensky Modulation Index Predicts Earlier Occurrence of Ventricular Arrhythmias In Patients With Implantable Cardioverter Defibrillators

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**Introduction:** Prediction of ventricular arrhythmic events (VA) is important in determining benefit

of ICD therapy. Wedensky modulation (WM) is a novel non-invasive tool that comprises subthreshold transthoracic electrical stimulation delivered to every other QRS complex. A WM index was computed from electrocardiographic differences between stimulated and non-stimulated complexes and has been shown to accurately predict VA events. We hypothesized that an increased index might predict early VA occurrence. Methods: R-wave WM index (WMIR) and combined RT-wave WM index (WMIRT) were prospectively evaluated from a prospective observational study at 8 international centers. The time from WM testing to VA occurrence, along with rate of the VA event, were compared to the WM indices. Results: A Low WMIRT was associated with longer time to VA event than a high WMIRT ( $183 \pm 107$  days versus  $148 \pm 108$  days ( $p=0.01$ )). Strong positive correlation between WMIR ( $p=0.03$ ) and WMIRT ( $p=0.003$ ) and the time from WM testing to initial VA event was determined. Patients with a positive index value ( $WMIR \geq 0.5$ ) were more likely to have a VA event sooner than patients with a negative index value ( $WMIR < 0.5$ ). There was a strong positive correlation between WMIRT and VA rate ( $p = 0.014$ ). Spontaneous VA rates were predicted as  $172 + (124 * WMIRT)$  days from WM testing for VA events in the first year ( $p = 0.008$ ). Conclusions: WM is a useful non-invasive tool that predicts earlier occurrence of VA events and more rapid spontaneous VA rate and may be helpful in determining which Pts are most likely to benefit from ICD therapy.