

Nuclear Cardiology and Cardiac CT

ESC Working Group



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MESSAGE FROM THE CHAIRMAN

Dear Friends,

The recent ESC Congress in Barcelona and the following Brainstorming meeting have been important occasions for the activities and vitality of the Working Group. The ESC meeting in Barcelona included several debates and symposia proposed by the WG spanning current and perspective applications of nuclear and CT imaging along the spectrum of cardiovascular diseases. In the following Brainstorming meeting several new methodological approaches have been reported for nuclear imaging and cardiac CT from different top imaging centers across Europe.



These activities reflect the increasing interest of the cardiological community for widespread and appropriate applications of cardiac imaging modalities and foster the role of our WG in addressing the increasingly perceived need of education and dissemination of cardiac imaging, especially among new young generation of cardiologists.

Sincerely,

Pasquale Perrone Filardi

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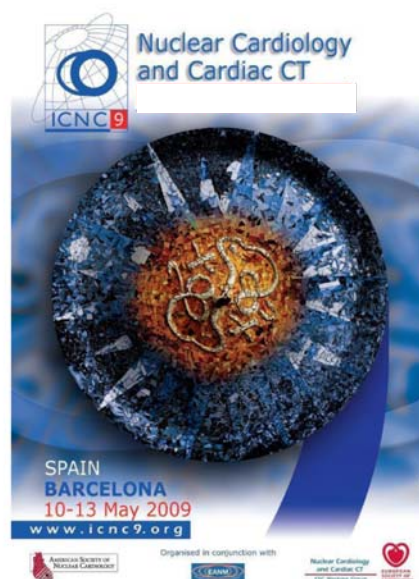
ICNC9; THE 9TH INTERNATIONAL CONFERENCE ON NUCLEAR CARDIOLOGY AND CARDIAC CT

Contributed by Juhani Knuuti; ICNC9 co-chair

Congress-co-chairs: Robert Hendel and Juhani Knuuti

Program committee chairs: Philipp Kaufmann, Frank Bengel and Gary Heller

ICNC9, the key international scientific meeting on Nuclear Cardiology and Cardiac CT, was taking place in Barcelona, 10-13 May. The ICNC was now in its 18th year and was highlighting cardiac CT and expanded information about cardiac PET in addition to the novel developments of SPECT. The scientific program structure was the familiar one with 4 parallel tracks: Essentials, Core Curriculum, Advances and Read with the Expert Sessions. These tracks were composed in a way that the participants focusing on cardiac CT could follow a CT program throughout the meeting. The program consisted of 285 original scientific and clinical contributions, including 42 oral abstracts.



This time the meeting was organized under dark financial clouds and, not enough, just before the event the crisis with H1N1 influenza started. As a meeting co-chair it was really a great pleasure to notice again that our biannual meeting is able attract so many people from so many countries worldwide despite the difficult times. We got over 900 participants in total which is not much less than the earlier meetings and from record high number of countries (75). The number of abstracts was almost 400 and the industry exhibition was large with 178 exhibitors.

Even more important, listening to the participants and their very positive feedback I felt proud of participating in organizing this event. Therefore, the decision to continue the ICNC congresses was easy. After careful comparison of several candidate cities, it was decided that ICNC10 will be arranged in Amsterdam in 2011. The organizing teams are just now being composed and the work for ICNC10 is starting. I will continue one more time as ICNC meeting co-chair, this time together with Rob Gropler and the program co-chairs will be Claudio Marcassa, Joanne Schuijff and Rob Beanlands.

SUMMARY OF HIGHLIGHTS OF THE 9TH INTERNATIONAL CONFERENCE ON NUCLEAR CARDIOLOGY AND CARDIAC CT



Barcelona, Spain May 10 – 13th, 2009

Contributed by:

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INTRODUCTION

The 9th bi-annual congress of the International Conference on Nuclear Cardiology (ICNC) was held in Barcelona, Spain from May 10th to 13th 2009. The total attendance was over 900 participants from 75 different countries. Excellent congress facilities hosted 43 prearranged sessions in 4 meeting rooms running in parallel. A total of 383 abstracts from 46 different countries were selected for presentation. The summary below is far from complete, but is focused on a few interesting presentations and developments in the field of nuclear cardiology and cardiac CT.

PROGNOSIS

The vast majority of myocardial perfusion studies are performed for prognostic purposes. During the ICNC meeting, a large amount of presentations were related to the topic of prognosis. The major session on prognosis was the Core Curriculum Session on “Risk assessment with non-invasive imaging”, which was chaired by Dr.

Perrone-Filardi and Dr. Allman. In this session the usefulness and potential value for risk stratification of currently available non-invasive cardiac imaging techniques was discussed. In an introductory presentation Dr. Polk discussed the background of non-invasive imaging for risk stratification and how the value of new imaging techniques for risk stratification should be interpreted. Several factors must be taken into account when reviewing the available data such as the accuracy of the test, the endpoints it predicts, the population in which it is used and if the prognostic information actually results in patient benefit. As a well validated and robust imaging technique, myocardial perfusion imaging with single photon emission computed tomography (SPECT) provides the benchmark against which new techniques should be judged.

Dr. Hendel led off the second presentation with an excellent overview of the available literature on the prognostic value of SPECT imaging. This functional imaging technique provides excellent prognostic value. A normal perfusion is associated with a very low event rate <1% annually, while an abnormal perfusion scan results in an almost 10-fold increase in event rate. Furthermore, the extent and severity of the abnormalities provide even further differentiation of risk. SPECT has many applications and its clinical value has been proven in many patient populations including stable chest pain, post myocardial infarction, post revascularization, pre-operative assessment, and in patients with cardiomyopathy, and there is a consistency of data over a long period of time. Finally SPECT has been shown to be cost-effective which enables this technique to be used as gatekeeper for further cardiac assessment.

In the third presentation the value of positron emission tomography (PET) imaging was reviewed by Dr. Neglia. PET has a high spatial resolution, reliable attenuation correction, low radiation dose, high diagnostic accuracy and allows for absolute quantification of myocardial blood flow. These advantages translate into a good prognostic value with a very low event rate in patients with normal perfusion. Quantification of myocardial perfusion allows for identification of disease at an earlier stage than SPECT by enabling assessment of endothelial dysfunction. As a result, this information may be used as an early predictor of events. However more data are needed on the prognostic value of PET for risk stratification. Currently two

large trials (SPARC and EVINCI) are on their way to further clarify the usefulness of PET in this regard.

Dr. Mahmarian discussed the value of calcium score (CS) testing for prognosis. CS allows for detection of subclinical disease and has the advantage of a rapid scan time, no patient preparation, availability on most computed tomography systems, low radiation burden and the ability to assess non-coronary causes of chest pain. The prognostic value of CS has been tested in over 70.000 patients and the absence of calcium has an excellent prognosis while the event rate increases in parallel to an increasing CS. This technique may be useful for screening, to determine the need for extra testing, to guide decision-making in patients with normal perfusion on SPECT and may also be useful in the emergency department for quick rule out of disease with good accuracy and high cost effectiveness.

In the final presentation, Dr. Bax discussed the value of multi-slice computed tomography coronary angiography (MSCT). This technique has a high accuracy for diagnosing the presence of significant >50% coronary artery stenosis. The negative predictive value of MSCT is especially high allowing accurate rule out of atherosclerosis. Only limited data are available on the prognostic value of MSCT. The preliminary data have shown that a normal MSCT has an excellent prognosis while increasingly severe disease results in increasingly higher event rates. Finally the anatomic information on MSCT has incremental prognostic value to perfusion imaging with SPECT, especially the presence of non-calcified plaque seems to provide important additional information.

During the ICNC 2009 congress several excellent abstracts were presented on risk stratification with nuclear imaging and on the prognostic value of multi-slice computed tomography coronary angiography. Chang et al. (1) assessed the incremental value of coronary artery CS to prognostic information obtained using myocardial perfusion imaging (SPECT). In 1035 generally asymptomatic subjects without prior cardiovascular disease CS added incremental value for predicting events over clinical and SPECT information. In patients with normal SPECT, CS added significant prognostic value 4 to 5 years after initial testing. These results support the role of CS testing in subjects with normal SPECT to clarify long-term risk. Van Werkhoven et al. (2) performed a study in 509 symptomatic patients undergoing

both MSCT and CS testing to identify if the additional anatomic information obtained with MSCT results in incremental prognostic value over CS. MSCT provided more detailed information on the presence and extent of atherosclerosis and after correcting for baseline risk factors and CS in a multivariate the information on MSCT remained an independent predictor, suggesting that MSCT may allow for more superior risk stratification compared to CS alone (Figure 1).

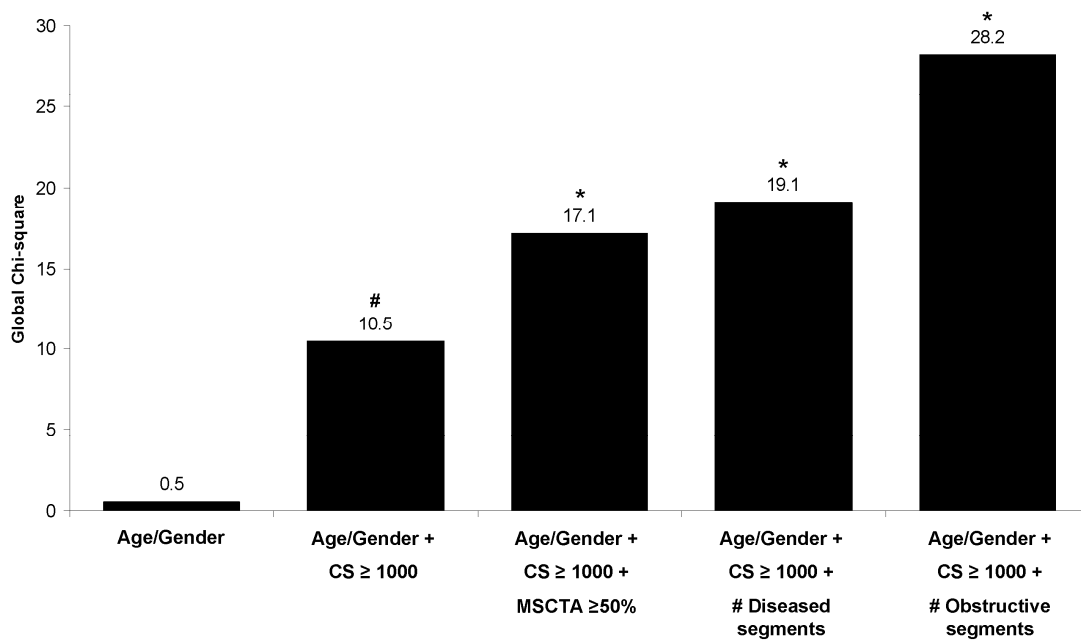


Figure 1. Bar graphs illustrating the incremental prognostic value (depicted by chi-square value on the y-axis) of obstructive ($\geq 50\%$) stenosis on MSCT and plaque burden (defined as the number of diseased or segments with obstructive stenosis on MSCT) over age, gender and CS. CS has a significant incremental prognostic value over age and gender (#). A further incremental prognostic value over age, gender and CS was observed with the addition of MSCT (*). Data from van Werkhoven et al. (2). Abbreviations: CS: calcium score; MSCT: multi-slice computed tomography

Stress-only SPECT perfusion imaging has the advantage of saving time and lowering the radiation exposure. However it remains unclear if a normal stress-only scan has the same low event rate as observed with traditional stress-rest protocols. Duvall et al.(3) compared the follow-up of 1673 patients who had a normal stress-only study

to 3237 who had a normal rest-stress study during a mean follow-up of 40 ± 9 months. The 1 year all-cause mortality rate was 1.3% in the stress-only group and 1.2% in the rest-stress cohort (Figure 2) A normal stress-only SPECT myocardial perfusion study therefore has an excellent 1 year prognosis.

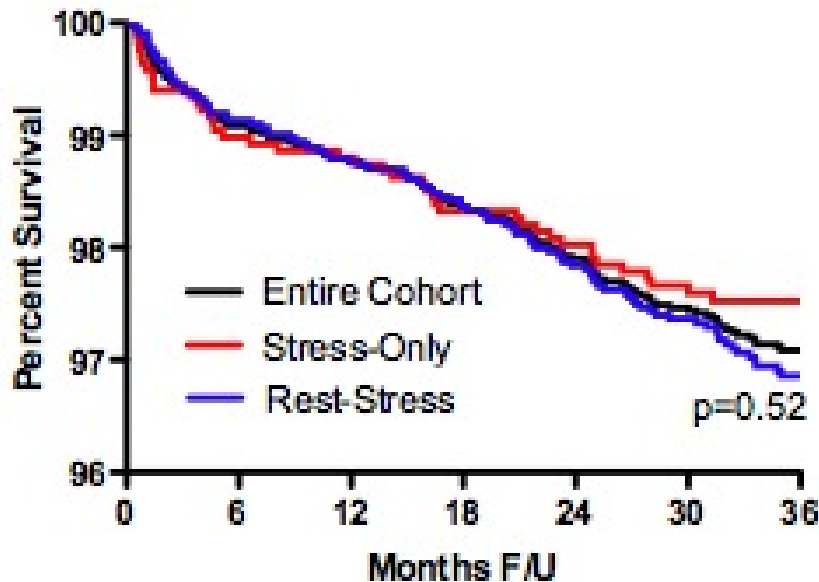


Figure 2. Kaplan-Meier survival curve depicting the prognostic value of a normal perfusion scan. No difference in survival was observed when comparing a stress-only protocol to a standard rest-stress protocol ($p=0.52$) Data from Duvall et al.(3).

Positron emission tomography allows assessment of both myocardial perfusion as well as coronary flow reserve (CFR). A PET study from Finland demonstrated that assessment of absolute perfusion and CFR were associated with significant coronary artery disease (4). Another study indicated that cardiac perfusion reserve assessed by PET was an indicator of microvascular disease reserve (5). The additional value of perfusion reserve over the traditional summed stress score was reported in a study from Canada using Rubidium-82 PET (6). In addition, it was shown that endothelial dysfunction can be detected easily with PET in patients with diabetes without significant atherosclerosis (7).

Herzog et al. (8) assessed the prognostic value of PET imaging and the added value of CFR assessment for the prediction of outcome. Perfusion and CFR was assessed in 256 patients using PET and ¹³N-ammonia. Both in patients with normal as well as in patients with abnormal perfusion an abnormal CFR was independently associated with a higher annual event rate compared to normal CFR (Figure 3). The addition of CFR measurements (which may indicate microcirculatory disease) increase the predictive value of PET.

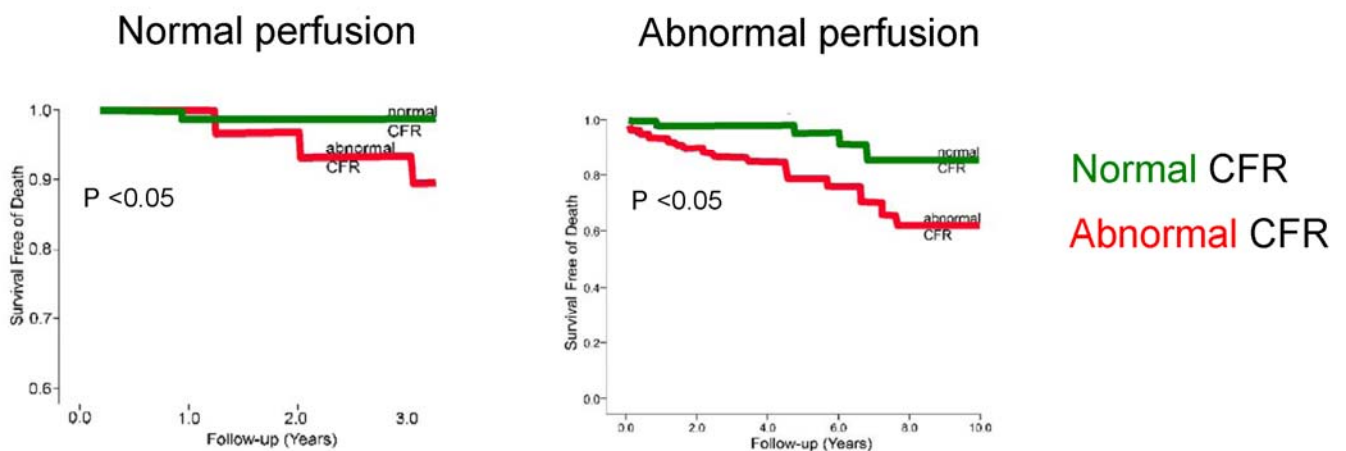


Figure 3. Prediction of cardiac death by CFR in patients with normal perfusion and in patients with abnormal perfusion. Data from Herzog et al. (8).

Abbreviations: CFR: coronary flow reserve.

MSCT

Another important topic at ICNC was the non-invasive assessment of the coronary arteries (and stenoses) using MSCT. In a poster session on CT angiography, the most recent advances in MSCT technology were addressed. The issue of radiation exposure during MSCT coronary angiography has been of recent concern because of the attributable risk of cancer. Accordingly, several abstracts focused on prospective ECG gating, for the purpose of radiation dose reduction for CT coronary angiography (CTA). Husmann et al. reported that CTA using prospective ECG-triggering may

significantly reduce patient radiation exposure (9). One hundred patients undergoing CTA using prospective ECG triggering (Figure 4) were compared to 100 patients who had previously undergone CTA using retrospective ECG gating. It was demonstrated that prospective ECG triggered triggering during CTA allows a reduction of radiation exposure by nearly 90%, with a mean total effective radiation dose of 2.2 mSv.

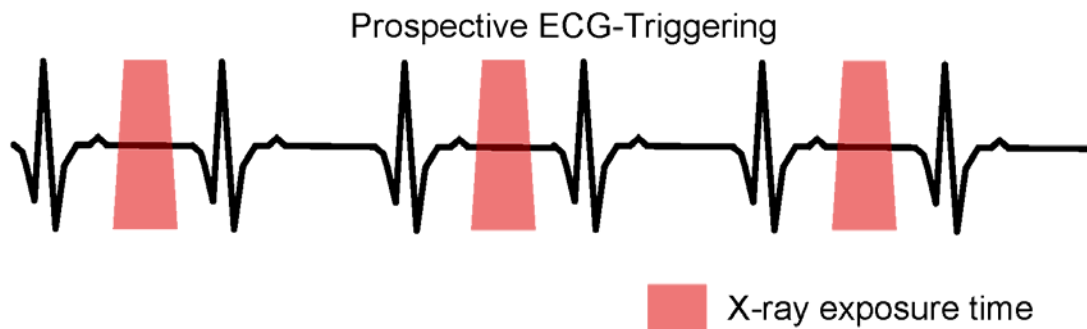


Figure 4. Prospective ECG triggering reduces X-ray exposure. Reproduced with permission from Husmann et al. (9).

Abbreviations: ECG: electrocardiogram.

Herzog and colleagues reported excellent accuracy of low dose CT coronary angiography using prospective ECG-triggering in a group of 30 patients (10). The investigators reported an estimated mean effective radiation dose of 2.1 mSv, while maintaining diagnostic image quality in 96% of segments. On a patient-basis, sensitivity, specificity, positive and negative predictive values were 100%, 83.3%, 90.0%, and 100%, respectively. Furthermore, the aforementioned group investigated the effect of mean heart rate and heart rate variability on prospectively gated CTA image quality. A total of 129 patients underwent CTA using prospective ECG triggering. It was found that this scanning technique indeed allows low dose CTA, but requires low heart rate, as prolonged diastole widens the optimal phase for scanning (11). Heart rate variability, however, was found to have only minimal impact on MSCT image quality.

Recently, 320-row systems have been introduced, allowing volumetric, single heart-beat image acquisition (Figure 5). Izumi and co-workers presented the novel features

of 320-row MSCT in comparison to 64-slice systems (12). A total of 30 patients underwent 320-row MSCT, and 45 patients underwent 64-slice MSCT. The group showed that scanning time in 320-row systems was significantly reduced, as compared to 64-slice MSCT (2.50 s vs. 7.84 s). In addition, 320-row MSCT provided high image quality with less contrast administration, when compared to 64-slice MSCT.

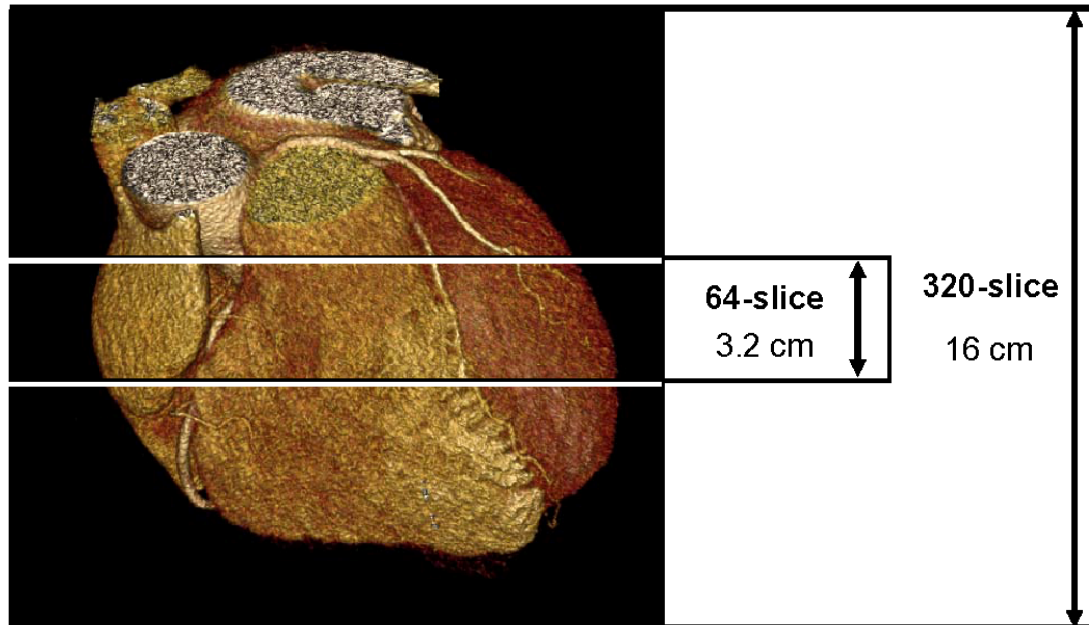


Figure 5. 320-row MSCT allows single rotation coverage of the entire heart.

Conversely, 64-slice CTA covers 3.2 cm in a single rotation. Reprinted with permission from de Graaf et al. (13).

Abbreviations: MSCT: multi-slice computed tomography.

Furthermore, in a moderated poster session addressing CT, de Graaf et al. presented the accuracy of left ventricular (LV) function assessment using 320-row MSCT, as compared to 2-dimensional echocardiography (13). CTA's were performed in a single heart-beat using prospective ECG-triggering and ECG dose modulation, scanning full dose during early diastolic phase. Good correlations between 320-row MSCT and two-dimensional echocardiography were demonstrated for the assessment of LV end-diastolic volume, LV end-systolic volume and LV ejection fraction (LVEF). LVEF was overestimated using MSCT by an average of 1.0%. Thus, accurate assessment of

LV function and volumes was shown to be feasible with 320-row MSCT in patients referred for MSCT coronary angiography.

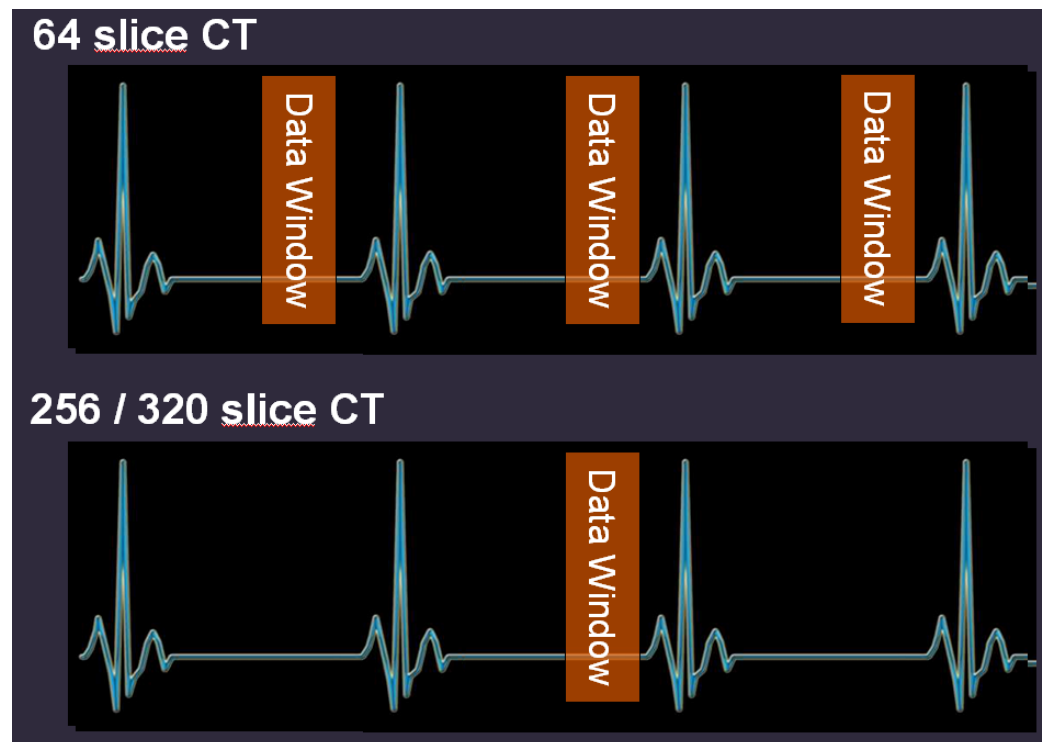


Figure 6. 64-slice CTA, with a cranio-caudal coverage of 3.2 cm in a single rotation, requires image acquisition of the entire heart in multiple heart beats. State of the art 320-row and 256-slice CTA, with a cranio-caudal coverage of 12.8 and 16 cm, respectively, allows image acquisition of the entire heart in a single heart beat. Reproduced with permission from Dr. Achenbach. Abbreviations: CT: computed tomography.

In a session addressing the *fundamentals of nuclear imaging and cardiac CT*, chaired by Dr. Freeman and Dr. Vassiliadis, Dr. Achenbach reviewed the topic *CT-coronary angiography: slices, sources, and scanning protocols*. It was discussed that 64-slice MSCT systems are the current standard for MSCT scanning. However, the development of wider CT detectors has led to shorter scan times (Figure 6) and less problems of image misalignment. Additionally, the development of dual source CT technology has greatly increased temporal resolution. Dr. Achenbach went on to discuss tips and tricks for MSCT scanning. The importance of proper patient

preparation was addressed, in particular using beta-blockers to reduce heart rate, the administration of nitrates, and the importance of breath-hold instructions to the patient to reduce motion artifacts. Subsequently, CT acquisition protocols and contrast administration were reviewed. The possibility of lowering the tube voltage from 120 kV to 100 kV was proposed, which may reduce radiation dose to up to 40%. In addition, prospective ECG triggering greatly reduces radiation-exposure. Furthermore, high contrast flow (5-7 ml/sec), followed by a saline flush, will provide good contrast enhancement which is essential for optimal image quality. Lastly, the importance of systematic post-processing was discussed, which should start with the assessment of axial slices followed by maximal intensity projections and curved multi-planar reconstructions.

In a session addressing *Advances in cardiac CT methodology*, chaired by Dr. Thomas and Dr. Mahmarian, the topic of prospective ECG triggering for CTA was addressed by Dr. Husmann. This new technique offers a tremendous reduction of radiation dose, with mean radiation doses varying from 2-4 mSv, depending on vendor, tube voltage and current, and padding. However, motion artifacts still occur, and the diagnostic accuracy of CTA using prospective ECG triggering remains similar to that of retrospectively gated image acquisition.

Subsequently, Dr. Schuleri addressed the topic *256-Slices and beyond*. In the past decade MSCT systems have advanced from 4- to 16- to 64-slices, and recently 256- and 320-slice systems were introduced. 256- and 320-slice systems have wide range coverage and can capture the entire heart in one or two rotations. Therefore these systems reduce total acquisition time as well as the problem of stair-step artifacts. Furthermore dual-source systems have been introduced, which have increased temporal resolution and allow CTA image acquisition with a total radiation dose of less than 1 mSv. In addition step-and-shoot cardiac scanning technology has become available, with automatic arrhythmia detection and correction. This technology can identify an arrhythmia, stop the scan, and rescan the anatomic region when the heart rate has stabilized. Lastly, the possibility of CT myocardial perfusion imaging (CTP) was discussed, which may detect transmural differences in myocardial perfusion. When combined with CTA, CTP has the potential to accurately predict atherosclerosis causing perfusion abnormalities. Both investigations may be

performed in a single examination of approximately 15 minutes, with a total patient radiation exposure of approximately 12 mSv.

Furthermore, the topic of *Dual-Source CT* was presented by Dr. Kopp. Challenges in cardiac CT have been mainly associated with limited spatial and temporal resolution, especially when compared to invasive coronary angiography. Recently, dual-source systems have been introduced which uses each of two tubes to acquire a quarter of a gantry rotation of data from the same heartbeat, thereby greatly increasing temporal resolution to up to 75 ms. Furthermore, these systems have better spatial resolution (0.3 mm). Specific advantages of dual-source scanning technique are that it allows single segment reconstruction for all heart rates and the temporal resolution is independent of heart rate. This technique allows good image quality even at increased heart rates, eliminating the necessity for heart-rate lowering premedication. Moreover, increased spatial resolution of dual-source CT reduces the problem of blooming artifacts, which may be caused by stents or calcium. Last, dual-source technology allows the implementation of dual-energy scanning techniques, which enhances tissue differentiation.

VULNERABLE PLAQUE IMAGING

Another topic of large interest is the non-invasive assessment of the vulnerable plaque; a main session was dedicated to this topic, entitled “Imaging of the vessel wall”. The first speaker was Dr. Fuster who provided an extensive overview of current imaging techniques for detecting the vulnerable plaque. As the vulnerable plaque is the most frequent cause of acute coronary syndromes there is an increasing clinical need for improved imaging techniques that can accurately identify this process. Dr. Fuster explained that the vulnerable plaque consists of a large necrotic core, macrophages and thin fibrous cap. First, he reviewed current investigational biology targeted at molecular imaging of the vulnerable plaque such as identifying LDL, HDL-c, leakage of red cells, inflammation and in particular imaging of macrophages. Consequently, he reviewed the different ways of detecting the vulnerable plaques invasively and non-invasively. Dr. Fuster concluded that non-invasive detection by multimodality plaque imaging techniques such as PET-CT with

F18-fluorodeoxyglucose (FDG) and magnetic resonance imaging (MRI) are the most promising techniques for the identification of the high risk plaques.

The second speaker was Dr. Thompson who discussed CT imaging of the vessel wall. He stated that more precise risk stratification of patients could be achieved by identifying *plaques* at high risk rather than *patients* at risk. Dr. Thompson considers that CT plaque imaging is promising for this very purpose. In addition, CT provides better discrimination of the atherosclerotic process than coronary angiography which only provides a two-dimensional luminogram. Additional factors influencing plaque vulnerability such as presence of positive remodeling, plaque volume and presence of spotty calcifications can also be assessed by CT. New techniques include Dual-Energy CT (DECT) which has the potential to provide additional attenuation data for better differentiation of plaque components. Dr. Thompson concluded that CT imaging provides accurate imaging of the atherosclerotic process including remodeling, extent and severity and that CT has the ability to discriminate between plaque compositions and assess presence of culprit lesions.

Lastly, MRI imaging of the vessel wall was reviewed by Dr. Botnar. MRI is one of the most exciting techniques for non-invasive molecular imaging of the cardiovascular system. This technique has a potential role in the early detection and better understanding of plaque biology in vivo. Additionally, effectiveness of pharmacological therapy can be assessed with this technique. Dr. Botnar reviewed the use of different contrast agents which can significantly increase the signal-to-noise ratio. In general, either T1 shortening contrast agents (e.g., based on Gadolinium), or T2 shortening contrast agents (e.g., based on iron oxides) can be used. The different plaque components related to plaque vulnerability can be selectively targeted (e.g. elastin, macrophages and fibrin). New techniques include delayed contrast enhancement cardiovascular MR imaging for plaque visualization in the coronary arteries. This technique has been successfully employed and shows high potential for the assessment of coronary disease of patients with subclinical and advanced atherosclerosis.

The last speaker was Dr. Hofstra who discussed the different radiotracers to characterize plaque biology and activity. According to Dr. Hofstra, current risk prediction in the general population is not sufficient and more precise identification

of patients at risk is needed. Currently, distinction between stable and unstable lesions is not yet feasible. Dr. Hofstra provided an overview of the emerging molecular targets available. Neovascularization can be identified by labeling vascular endothelial growth factor with 99m-technetium. In addition, inflammation, in particular macrophages, can be identified by labeling matrix metalloproteinases, FDG and monocyte chemoattractant protein. Apoptosis can be accurately identified using molecular targets such as Annexin A5 and Caspase. Indeed, a number of successful preclinical concepts have been provided, however, only a limited number translate to clinical studies. Large prospective trials are needed to improve the incremental value of radiotracers in the near future.

INNERVATION IMAGING

The last topic that attracted a lot of attention was cardiac innervation imaging. Dr. Carrio presented an excellent review of the role of sympathetic nerve imaging in evaluation of cardiac patients. Initially, an overview of the basic principles of the most commonly used cardiac sympathetic nerve tracer metaiodobenzylguanidine (MIBG) was provided. Subsequently, Dr. Carrio reviewed the potential clinical role of cardiac sympathetic nerve imaging with MIBG in prediction of ventricular arrhythmias and cardiac death. With respect to prediction of ventricular arrhythmias, it has been shown that patients with appropriate implantable cardioverter defibrillator (ICD) therapy had significant lower cardiac MIBG uptake on late planar imaging as compared to patients with appropriate ICD therapy. Besides global MIBG uptake, Dr. Carrio showed that regional MIBG uptake as assessed with SPECT imaging could be of potential use in prediction of ventricular arrhythmias. For example, it has been demonstrated that patients with positive electrophysiologic testing (inducible ventricular tachy-arrhythmias) had significantly more MIBG regional defects than patients without positive testing. Furthermore, Dr. Carrio discussed the role of MIBG imaging for risk stratification of heart failure patients. He showed that presently a substantial amount of evidence exists on the predictive value of cardiac MIBG imaging in heart failure patients: the survival rate in patients with high cardiac MIBG uptake is significantly higher as compared to patients with

low cardiac MIBG uptake. These findings have consistently been reported by single center trials and confirmed by multi-center studies. In addition, studies have shown that MIBG imaging can be used to evaluate effects of medical therapy. Indeed, increased cardiac sympathetic innervation could be demonstrated after beta-blocker therapy and cardiac resynchronization therapy (CRT).

Sudden cardiac death represents an important health care problem in terms of morbidity and mortality numbers. The MADIT II trial has demonstrated that ICD treatment is indicated in patients with moderate-to-severe heart failure and poor LV systolic function (LVEF $\leq 35\%$) as primary preventive therapy. However, a large number of patients (stratified according to current ICD selection criteria) do not receive appropriate ICD therapy (shocks or anti-tachycardia pacing) during follow-up, and refinement of selection criteria for ICD implantation may be needed. The MIBG Leiden Study evaluated whether cardiac sympathetic innervation assessed with MIBG scintigraphy is related to appropriate ICD therapy (primary endpoint) or the composite of appropriate ICD therapy or cardiac death (secondary endpoint).

The study included more than 100 patients undergoing cardiac MIBG imaging and myocardial perfusion imaging before ICD implantation. Patients were followed-up from ICD implantation to first documented appropriate ICD therapy (primary endpoint) or appropriate ICD therapy or cardiac death (secondary endpoint).

Multivariable analysis demonstrated that late MIBG SPECT defect score was the only independent predictor for appropriate ICD therapy (primary endpoint) and appropriate ICD therapy or cardiac death (secondary endpoint). These results are promising for the use of MIBG imaging in selection of ICD therapy, but more studies are needed on this topic.

Dr. Agostini presented the ADMIRE-HF trial, a prospective multicenter trial (96 centers) evaluating the prognostic value of MIBG imaging in heart failure patients. The primary objective of the study was to demonstrate the prognostic value of cardiac sympathetic innervation as assessed with heart-to-mediastinum (H/M) ratio on planar imaging. Cardiac sympathetic innervation was defined as normal (>1.6 H/M ratio) or abnormal (<1.6 H/M ratio). The secondary objective of the ADMIRE-HF trial was to establish the value of MIBG imaging for quantification of the risk for heart failure progression, arrhythmic events or cardiac death. In this study, 961

patients with advanced heart failure (New York Heart Association (NYHA) functional class II/III) and poor LV systolic function (LVEF \leq 35%) were included. Patients were followed-up for a maximum of two years. Primary study endpoint was defined as the first occurrence of either: heart failure progression, arrhythmic event (sustained ventricular tachyarrhythmia, appropriate ICD therapy or aborted cardiac arrest) or cardiac death. In total, 238 (25%) patients had an adverse cardiac event, including heart failure progression (n = 163), arrhythmic event (n = 51) and cardiac death (n = 24). Consecutively, Dr. Agostini showed that patients with normal cardiac sympathetic innervation (H/M ratio $>$ 1.60) showed significant higher event-free survival as compared to patients with abnormal cardiac sympathetic innervation (H/M ratio $<$ 1.6) (2-year event-free survival 85% vs. 63%, $p <$ 0.01). In addition, Dr. Agostini showed a separate survival curve analysis for heart failure progression, arrhythmic events and cardiac death. Event-free survival was significantly higher in patients with H/M ratio $>$ 1.6 than patients with H/M ratio $<$ 1.6 using heart failure progression, arrhythmic events or cardiac death as an endpoint.

Subsequently, the multivariable analysis showed that LVEF, BNP and late H/M ratio were independent predictors for adverse cardiac events. However, even in patients with severely depressed LVEF or abnormal BNP levels, event-free survival was significantly higher in patients with normal cardiac sympathetic innervation than patients with abnormal cardiac sympathetic innervation.

Various abstracts on the use of MIBG imaging were presented at ICNC. Verschure et al. (14) presented on the predictive value of MIBG scintigraphy in patients with chronic heart failure. In total, 39 patients with heart failure (24 men, mean age 64 ± 11 years, mean LVEF $24 \pm 12\%$) were studied. During follow-up (60.1 ± 37.2 months) 6 cardiac deaths were documented. From MIBG imaging, early and late H/M ratios and washout were calculated. In addition, renal function was calculated using the Cockcroft-Gault formula and the abbreviated MDRD-formula. Using multivariable cox hazards regression analysis, the authors demonstrated that late H/M was the only independent predictor for cardiac death.

Parades Rodriguez et al. (15) performed MIBG imaging before and after CRT; 12 patients with chronic heart failure meeting conventional criteria for CRT were prospectively studied. All patients underwent planar and SPECT MIBG imaging before

CRT, and nine patients underwent MIBG imaging at least 6 months after CRT. In addition, clinical and echocardiographic response was determined after CRT. The late H/M ratio showed improvement in five patients after CRT, which was accompanied by clinical and echocardiographic response to CRT.

Rahbar et al. (16) studied the potential influence of adrenergic dysfunction on arrhythmic events in patients with arrhythmogenic right ventricular cardiomyopathy (ARVC). Ventricular tachyarrhythmias can be induced by stress or catecholamines indicating a potential role of the cardiac adrenergic system in the arrhythmogenesis. Abnormalities of the presynaptic uptake-1 assessed MIBG scintigraphy have been demonstrated in previous studies. In 42 patients with ARVC (mean age 43 ± 14 years), MIBG SPECT imaging was performed. The findings were compared to those obtained from 10 control subjects (mean age 43 ± 12 years) without identifiable structural heart disease. Abnormal tracer uptake was detected in 25 (59%) patients with ARVC. Patients with an abnormal MIBG SPECT study showed significantly more life-threatening ventricular tachyarrhythmias as compared to patients with normal sympathetic innervation during long-term follow-up of 9.2 ± 3.4 years (84% vs. 41%; $P < 0.01$) (Figure 7).

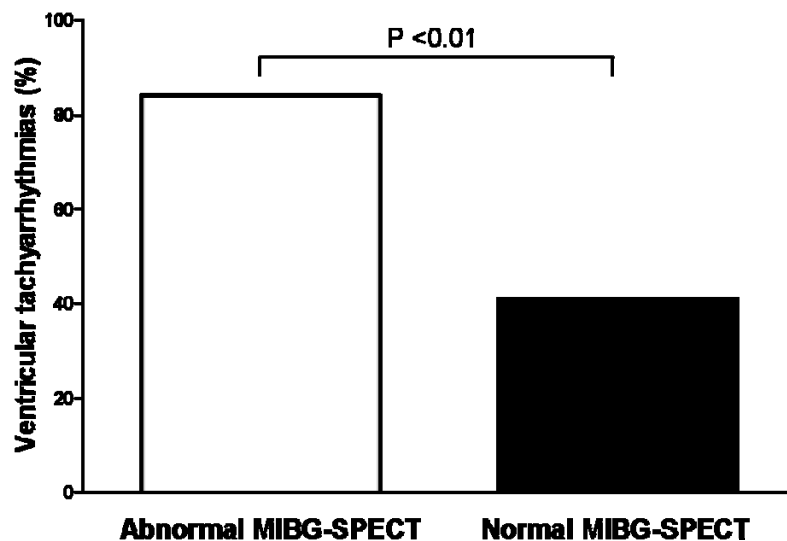


Figure 7. Patients with an abnormal late MIBG SPECT showed significantly more life-threatening ventricular arrhythmias as compared to patients with a normal late MIBG SPECT (84% vs. 41%, $P < 0.01$) during long-term follow-up of 9.2 ± 3.4 years. Bar graph reconstructed with data from Rahbar et al.(16).

These findings suggest that adrenergic dysfunction in patients with ARVC appears to be associated with a higher risk for ventricular tachy-arrhythmias recurrences. Moreover, the authors suggested that MIBG SPECT imaging may have a role in risk stratification of patients with ARVC.

YOUNG INVESTIGATOR AWARD SESSION

Five of the best abstracts submitted by young investigators were presented in the Young Investigators Award Oral Abstract session. The winning abstract, presented by S. Javadi and colleagues, sought to test the potential of CFR to detect risk for events in patients referred for clinical Rb-82 myocardial perfusion PET-CT (5). In total, CFR was quantified in 73 consecutive patients with chest pain and intermediate pre-test likelihood of coronary artery disease. Among 37 patients with atherosclerosis without ischemia, 17 (46%) had reduced CFR. During a mean follow-up of 296 ± 189 days, 15 patients had events (re-admission for chest pain $n = 9$; need for invasive coronary procedure $n = 5$; myocardial infarction $n = 1$); CFR was higher in patients with events versus patients without events (Figure 8). The authors concluded that quantification of CFR identifies prognostically relevant microvascular dysfunction in patients with atherosclerosis without ischemia.

Yoneyama and co-workers reported on a study comparing ^{123}I -beta-methyl-iodophenyl pentadecanoic acid (^{123}I -BMIPP) scintigraphy results between patients with vasospastic angina (VSA) with or without total coronary occlusion during acetylcholine provocation test (17). In total, 13 controls and 22 patients with VSA were studied. VSA patients were divided into two groups; the incomplete ($<90\%$ of luminal narrowing, $n = 7$; i-VSA) or complete coronary occlusion group ($n = 13$; c-VSA) during acetylcholine infusion. Significant differences were demonstrated in BMIPP parameters between the controls and total VSA group, but no differences were demonstrated between the i-VSA group and c-VSA group.

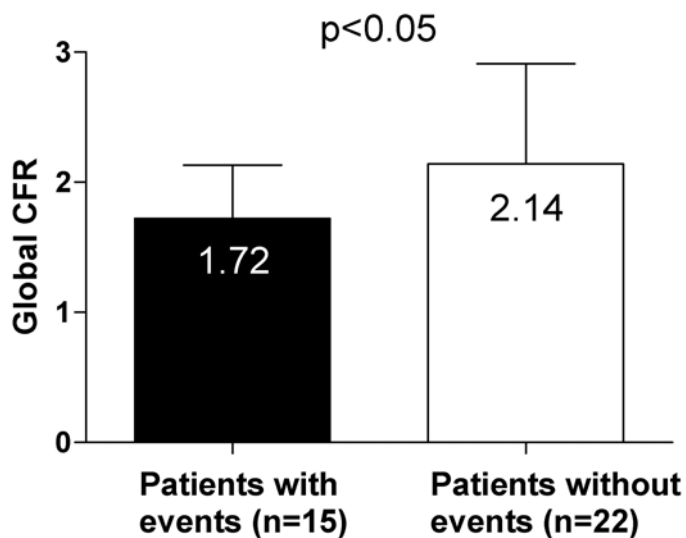


Figure 8. Bar graph representing the global coronary flow reserve (CFR) as quantified from Rb-82 PET-CT which was significantly lower in patients with events versus patients without events. Bar graph reconstructed with data from Javadi et al (5).

Kashiwagi and colleagues presented results evaluating the thin-capped fibroatheroma on MSCT as compared to invasive optical coherence tomography (OCT) in 42 patients (18). The authors demonstrated that MSCT could identify differences in plaque morphologies between TCFA's (thin capped fibroatheroma's) and non-TCFA's such as positive remodeling, low attenuation and a ring-like signal. Ali and colleagues evaluated the test-retest repeatability of myocardial SPECT perfusion in 2 different acquisitions on the same camera and processed with clinically used filtered backprojection (FBP) and iterative reconstruction with and without CT-based attenuation correction (19). Test-retest repeatability showed excellent reproducibility in 98/100 cases with only 2% discordance. This repeatability was maintained with iterative reconstruction with and without CT-based attenuation correction.

The last abstract, presented by George and colleagues, discussed myocardial sympathetic function in heart failure patients who recover on Left Ventricular Assist Device (LVAD) therapy (20). The authors studied cardiac sympathetic innervation using MIBG scintigraphy in patients during LVAD therapy, and in patients who had

had LVAD explanted following myocardial recovery. Compared with early post-implantation LVAD patients, long-term explanted group had significantly higher early H/M ratio and lower washout rate. The authors concluded that MIBG uptake improves with LVAD and intensive drug therapy in heart failure patients who recover and can be explanted and that MIBG scintigraphy could provide useful prognostic information and may guide device explantation.

CONCLUSION

The current summary has aimed to provide a selection of topics of interest presented at the 9th ICNC meeting in Barcelona 2009. Excellent overview lectures were provided and interesting new scientific were presented. The field of nuclear cardiology and cardiac CT is developing at a rapid pace, with significant advances in technology, equipment, tracers, and clinical applications.

The next ICNC meeting is scheduled in Amsterdam, The Netherlands, from May 15th to 18th, 2011.

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EVINCI NEWS

Contributed by Danilo Neglia, MD, PhD

Advancements

1. The WEB Site for Patients Enrollment is operative.
2. The Standardization Procedures have been successfully completed with issuing of standardized procedures for all non-invasive and invasive imaging modalities.
3. Official local Ethical Committee's Approval has been obtained in several centers and the first patients have been enrolled.
4. New centers have been contacted to join the Consortium and agreements are on going.
5. December 4-5, the first EVINCI meeting will be held in Pisa (see section upcoming events at page 26).

ESC TRAINING COURSE IN NUCLEAR CARDIOLOGY AND CARDIAC CT IN CLINICAL PRACTICE

Contributed by Joanne Schuijf, PhD

28-30 May 2009

Sophia Antipolis, France

With approximately 90 participants and 10 faculty members, the annual training course, which took place at the European Heart House in late May, was again considered a great success.

The basics and clinical aspects of nuclear cardiology and cardiac CT were covered by Drs Underwood, Reyes, de Feyter, Kaufmann, Bax, Wackers and Germano followed by discussion of the use of these techniques in various clinical settings. In addition, more advanced imaging techniques, such as molecular imaging or hybrid approaches, were covered by Drs Bax, Knuuti and de Feyter. The Read with the Experts sessions with Drs Germano, Harbinson, Kaufmann and Schuijf were highly appreciated. The interactive setting allowed discussion of clinical cases highlighting the strengths and pitfalls of the various techniques in daily clinical routine. Finally, the traditional variation on this theme entitled "Stump the Stars" had a number of the stars of nuclear cardiology and cardiac CT testing their reporting skills on unknown cases presented by the audience and their co-stars.

ESC TRAINING COURSE IN NUCLEAR CARDIOLOGY AND CARDIAC CT IN CLINICAL PRACTICE (CONTINUED)



UPCOMING EVENTS AND INTERNATIONAL MEETINGS

Certification Examination for Nuclear Cardiology 2009

This certification exam is arranged yearly (since 2004) by the Certification Board of Nuclear Cardiology (CBNC), in cooperation with the European Council of Nuclear Cardiology (ECNC).

The ESC Workgroup on Nuclear Cardiology and Cardiac CT and ECNC are very pleased to invite all qualified physicians to sit for the sixth CBNC (Certification Board of Nuclear Cardiology) certification examination for Nuclear Cardiology and Cardiac CT to be held in Europe, scheduled for Monday 30 November - Saturday 6 December, 2009.

The ESC Working Group on Nuclear Cardiology and Cardiac CT and ECNC strongly recommend that all European physicians, who are active in Nuclear Cardiology and Cardiac CT and eligible take this exam.

The exam is a benchmark of quality in Nuclear Cardiology and Cardiac CT in Europe!

To obtain specific information, please contact Susanna Wiener at ecnc-office@vereint.com or Dawn Edgerton at info@cbcct.org, or go to CBCCT [website](#)

EVINCI meeting “Multi-imaging in Cardiology”

4-5th December

Pisa, Italy

For more information, please e-mail to EVINCI@GASTALDI.IT

Nuclear Cardiology in Practice

Week 1 (Royal Brompton Hospital, London, UK) 1st – 5th February 2010

Week 2 (Harefield Hospital, Middx, UK) 8th – 12th February 2010

For more information, please e-mail to K.DIXON@IMPERIAL.AC.UK

First European Scientific Meeting of the SCCT

February 6th 2010

Leiden, the Netherlands

For more information, please e-mail to EUROSCCT@LUMC.NL or go to WWW.SCCT.ORG

More information on the individual meetings is attached.

- | | | |
|------|------------------|--------------------------|
| C. | Anagnostopoulos | London, UK |
| S. | Berti | Pisa, Italy |
| M. | Bertini | Leiden, Netherlands |
| P. | Camici | London, UK |
| C. | Carpeggiani | Pisa, Italy |
| G. | Casolo | Viareggio, Italy |
| D. | Chiappino | Massa, Italy |
| F. | Crea | Rome, Italy |
| V. | Di Bello | Pisa, Italy |
| M. | Di Carli | Boston, Ma, Usa |
| L. | Donato | Pisa, Italy |
| M. | Emdin | Pisa, Italy |
| F. | Falaschi | Pisa, Italy |
| C. | Fernández-Golfín | Madrid, Spain |
| M. | Ferrarini | Pisa, Italy |
| A. | Flotats | Barcelona, Spain |
| G.F. | Gensini | Florence, Italy |
| A. | Gimelli | Pisa, Italy |
| M. | Glauber | Massa, Italy |
| E. | Gronza | Milan, Italy |
| B. | Herzog | Zurich, Switzerland |
| J. | Knuuti | Turku, Finland |
| A. | L'Abbate | Pisa, Italy |
| D. | Le Guludec | Paris, France |
| A. | Lerman | Rochester, MN, Usa |
| U. | Limbruno | Grosseto, Italy |
| M. | Lombardi | Pisa, Italy |
| G. | Mariani | Pisa, Italy |
| P. | Marraccini | Pisa, Italy |
| M. | Marzilli | Pisa, Italy |
| P. | Marzullo | Pisa, Italy |
| M. | Mascalchi | Florence, Italy |
| M. | Mazzanti | Ancona, Italy |
| N. | Mazzuca | Grosseto, Italy |
| R. | Melandri | Pisa, Italy |
| A. | Morales M. | Pisa, Italy |
| D. | Neglia | Pisa, Italy |
| S. | Nekolla | München, Germany |
| L. | Padeletti | Florence, Italy |
| O. | Parodi | Pisa and Milan, Italy |
| P. | Perrone-Filardi | Naples, Italy |
| A.S. | Petronio | Pisa, Italy |
| E. | Picano | Pisa, Italy |
| F. | Rademakers | Leuven, Belgium |
| F. | Recchia | New York and Pisa, Italy |
| O. | Rimoldi | London, UK |
| D. | Rovai | Pisa, Italy |
| G. | Sambuceti | Genoa, Italy |
| J. | Schuijf | Leiden, Netherlands |
| J. | Schwitzer | Zurich, Switzerland |
| R. | Sciagrà | Florence, Italy |
| R. | Sicari | Pisa, Italy |
| A. | Teresinska | Warsaw, Poland |

MULTIMAGING IN CARDIOLOGY

CONGRESS VENUE

All scientific sessions will take place at:
 CNR - Area della Ricerca di Pisa
 Via G. Moruzzi, 1 - 56124 Località S. Cataldo - Pisa - Tel. +39 050 3152216

CME – CONTINUING MEDICAL EDUCATIONAL

The Meeting has been submitted for approval for Continuing Education Units to the Italian Ministry of Health. For Italian Doctors only

REGISTRATION FEE

The Registration Fee of 60,00 € (VAT 20% included) includes: entry to all the scientific sessions, badge and congress kit, attendance and CME certificates, coffee breaks and lunch. The Registration Form and the receipt of the bank payment should be sent to the Organizing Secretariat before 23rd November, 2009. After the deadline, all registrations will only be accepted at the Congress registration Desk upon availability. Cancellation received before November 23rd 2009 will be refunded less 50% for administrative costs. Cancellations received after that date, will not be refunded

OFFICIAL LANGUAGES

The official languages of the Congress are Italian and English.

SCIENTIFIC SECRETARIAT

Danilo Neglia, Rosa Sicari, Massimo Lombardi
 Istituto di Fisiologia Clinica del CNR
 Fondazione Toscana Gabriele Monasterio - Area della Ricerca di Pisa
 Via G. Moruzzi, 1 - 56124 Località S. Cataldo - Pisa

ORGANIZING SECRETARIAT

Congresship
 Mura di Santa Chiara, 1 - 16128 Genova
 Tel. +39 010 5999500 - Fax +39 010 5999499 - e-mail: evinci@gastaldi.it

The Research Leading to These Results Has Received Funding from The European Community's Seventh Framework Programme (fp7/2007-2013) under Grant Agreement n° 222915

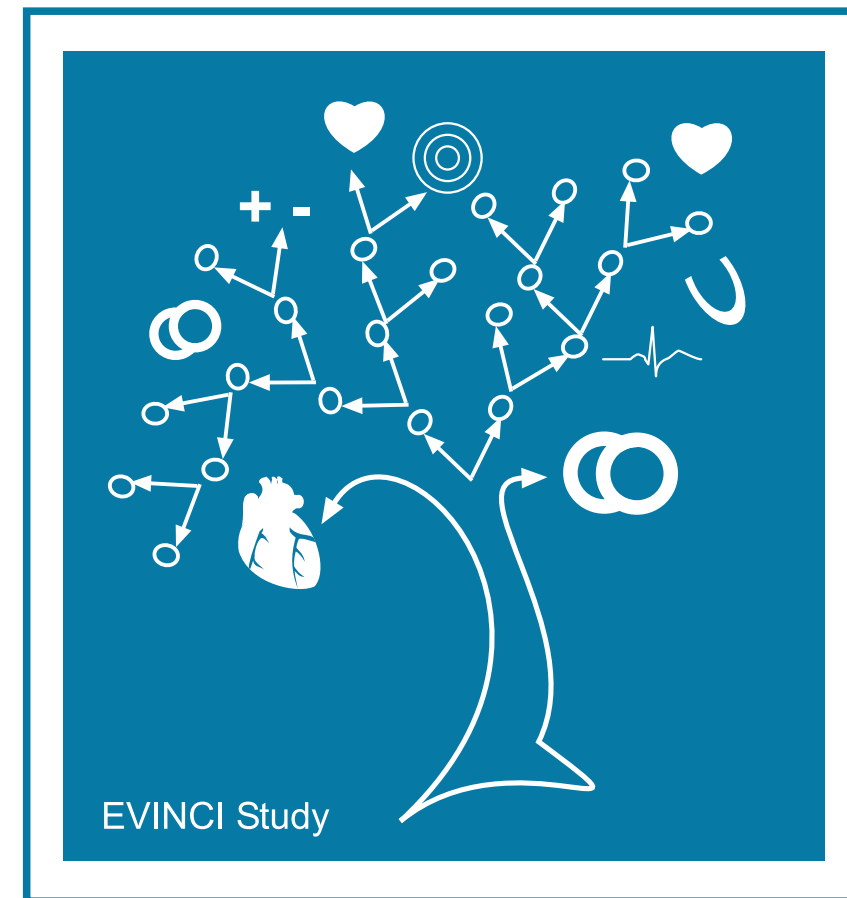
Supported by an Unrestricted Educational Grant From:

GE HEALTH CARE

MULTIMAGING IN CARDIOLOGY

Pisa - Area della Ricerca del CNR

4th - 5th December 2009



Endorsed by

e-mail: evinci@gastaldi.it

NATIONAL HEART AND LUNG INSTITUTE

Faculty of Medicine, Imperial College

Nuclear Cardiology in Practice

Week 1 (Royal Brompton Hospital, London) 1st – 5th February 2010
Week 2 (Harefield Hospital, Middx) 8th – 12th February 2010

Course Organisers:

Dr. Andrew Kelion
Prof. S Richard Underwood

Now in its 10th year, this popular two-week course aims to provide a thorough grounding in the theoretical and practical aspects of nuclear cardiology, involving both lectures and practical exposure. Both weeks will be suitable for professionals involved in using or delivering a nuclear cardiology service, whether medical, nursing or technical. Attendance at both weeks is desirable for a thorough grounding in the subject but attendance at either week alone is an option

Please note places are strictly limited to 20.

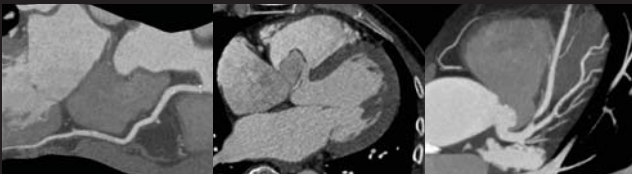
Course Fees:

Medical staff: 1 Wk £600; 2 Wks £950.
Non-medical staff: 1 Wk £475; 2 Wks £775

For further information & a registration form, please contact:

Karina Dixon, Events Office, National Heart & Lung Institute
Dovehouse Street, London SW3 6LY UK E-mail: k.dixon@imperial.ac.uk
Tel: +44 (0)20 7351 8172 Fax: +44 (0)20 7351 8246
http://www1.imperial.ac.uk/medicine/about/divisions/nhli/nhli_events/

First European Scientific Meeting of the Society of Cardiovascular Computed Tomography (SCCT)



Dear Colleagues,

It is our great pleasure to invite you to the First European Scientific Meeting of the Society of Cardiovascular Computed Tomography (SCCT), to be held in Leiden, the Netherlands on February 6, 2010.

The field of cardiovascular CT has experienced a rapid development during the past years. Consequently, the Society of Cardiovascular Computed Tomography is planning to strengthen its efforts in Europe and has established a committee to specifically promote and develop cardiovascular CT in European countries by supporting research, education and clinical excellence in the field.

The aim of this international one-day meeting is to provide a discussion of recently published guidelines and recommendations concerning cardiovascular CT as well as potential applications in daily clinical practice. In addition, smaller read with the experts sessions – tailored to different levels of experience in cardiovascular CT – will allow enhanced interaction between faculty and attendees. A detailed program will become available in autumn 2009.

Who should attend?

The meeting is aimed at cardiologists, radiologists, residents in training and other physicians with an interest in cardiovascular CT.

Venue

Leiden University Medical Center
Lecture Hall 3
Albinusdreef 2
2333 ZA, Leiden
The Netherlands

When?

February 6, 2010
9 am – 5 pm

We look forward to welcoming you in Leiden.

Joanne Schuijf, PhD
Leiden, The Netherlands

Martin Hoffmann, MD
Ulm, Germany

Stephan Achenbach, MD, FSCCT
Erlangen, Germany

Jörg Hausleiter, MD
Munich, Germany

Fee

Physician, Scientist, Industry, SCCT Member	€50
Physician, Scientist, Industry, Non-Member	€100
Resident or fellow in training, SCCT Member	€25
Resident or fellow in training, Non-Member	€50

To register as fellow, a written statement from the head of the department will be necessary.

Fee includes educational material, coffee breaks and lunch.

Information

Please go to www.scct.org for further information or express your interest by sending an e-mail to EuroSCCT@lumc.nl.



LEIDEN UNIVERSITY MEDICAL CENTER



SOCIETY OF
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