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D3.3 Medical application of ionising radiation and radiation protection in cardiovascular diseases

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Abbreviations

echo: echocardiography

CCT: cardiovascular computed tomography

CMR: cardiovascular magnetic resonance

SPECT: single-photon emission computed tomography

PET: positron emission tomography

EP: electrophysiology

EACVI: European Association of CardioVascular Imaging

CVD: Cardiovascular disease

Disclaimer

The opinions stated in this report reflect the opinions of the authors and not the opinion of the European Commission.

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I. Introduction

In the past decades, the diagnostic approach to cardiovascular diseases has been largely revised by the growing role of non-invasive imaging technologies, such as echocardiography (echo), cardiovascular computed tomography (CCT), cardiovascular magnetic resonance (CMR), single-photon emission computed tomography (SPECT), and positron emission tomography (PET) and invasive technologies (invasive coronary angiography and electrophysiology - EP). In addition to the relevant benefits and technical improvements in each of these modalities, great efforts have been made to broaden clinical indications, demonstrate accuracy and prognostic utility, and improve safety profiles.

During the past 10 years, numerous technologies and data acquisition protocols for low-dose imaging have become available. The implementation of these technologies is always a balance between the long-term risk associated with exposure to ionizing radiation and the short-term risk related to impaired diagnostic accuracy. Furthermore, an important aspect to keep the dose as low as possible is to choose the most appropriate test for an individual patient using the correct acquisition protocol: the evaluation of the most appropriate test, accordingly to clinical characteristics and anamnestic reports can be considered one of the pillars of personalized medicine and should be always keep in mind to improve the safety of the patients. From a clinical point of view, this implies to select the diagnostic test that is most likely to influence and direct patient care to improve outcome. From a technical point of view, this implies knowledge on differences between protocols and applying the protocol that results in the highest diagnostic performance with the lowest radiation exposure. Dose reduction is a multidisciplinary effort.

In this respect, the EURAMED rocc-n-roll project yields a strategic research agenda in the field of medical applications of ionising radiation and related radiation protection through a thorough analysis of research and radiation protection needs in the clinical cardiology using ionising radiation.

II. Literature review

Due to the importance of this topic, in the recent 5 years, several studies and recommendation papers focused on the evaluation of radiation dose in cardiac evaluation by non-invasive and invasive imaging techniques.

We identified the different application of radiation in cardiac disease: cardiac/cardiovascular CT, Nuclear cardiology (SPECT and PET), invasive cardiac imaging (cath lab, EP lab). Moreover, despite cardiac magnetic resonance (CMR) is a non-ionising radiation technique, we decided to include it in the evaluation process, also. As a matter of fact, CMR cannot be considered without problems and side effects. As previously demonstrated, unenhanced CMR is associated with minor but significant immediate blood cell alterations or activations figuring inflammatory response, as well as DNA damage in T lymphocytes observed from day 2 until the first month but disappearing at 1-year follow-up. Accordingly, further studies are required to definitely state whether CMR can be used safely, in particular for the CMR >3Tesla (1-4).

We evaluated the state of the art of the technical guidelines of CT, SPECT, PET and CMR, to evaluate the optimization protocol and the assessment of technology specific optimization (scanner generation, specific technical features,…). In addition, we identified the state of the art of the acquisition and data processing for diagnostic reference levels (5-19).

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Moreover, we looked at recent clinical data and in particular, at the EURECA (EUROPEAN REGISTRY ON CARDIOVASCULAR IMAGING) registry results. EURECA (EHJ accepted paper, in press) is an international registry proposed by the European Association of CardioVascular Imaging (EACVI). The aim of the registry is to evaluate the use of non-invasive cardiac imaging in a contemporary large population of patients with stable symptoms potentially caused by underlying obstructive coronary artery disease (CAD). The factors conditioning adherence to guidelines (20), local variability in the use of different modalities and possible effects on patient management will be assessed. The availability of radiation dose, requested for each modality, will allow to define the state of the art of the mean radiation dose of the different imaging techniques across Europe, but more than this, to evaluate the appropriate use of imaging technique, according to the most recent guidelines, and, eventually, to highlight the necessity to increase the attention of the not-appropriate use, that can increase the radiation burden. Analyses of the EURECA data about the mean radiation dose in different centres in EU for imaging technique are in progress, and they could be used to fill the gap on the state of the art of routinely clinical protocols.

New data on paediatric patients would be of interest. As a matter of fact, no data on radiation safety for the evaluation of paediatric patients with cardiac disease are available in the last years. The EPI-CT study may provide important information (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6469297/), despite this registry is not focused on cardiac evaluation but on cancer disease. Furthermore, a new EU consensus statement between the different cardiological associations was published to reinforce the attention of the cardiological community of the necessity to implement all the strategy to reduce radiation dose.

The use of novel molecular imaging methods, such as positron emission tomography, is now increasing and offers something different and complementary to the other techniques due to the ability to assess *disease activity* as it is occurring in patients. In principle, the activity of any pathological process can be targeted at the cellular or molecular level, although in practice this has been limited by the availability of appropriate tracers. In the last few years, there has been a dramatic expansion in radiotracer development that now allows the targeting of most pathological processes underlying cardiovascular disease including inflammation, infection, fibrosis, calcification and thrombosis. We discussed the established and novel radiotracers that can be used to assess disease activity in patients with cardiovascular disease and how these might aid clinical practice in a new era of targeted molecular imaging. Other methods of e.g. X-ray based molecular imaging might offer additional options for higher spatial or temporal resolution in molecular imaging, which might improve options for better understanding of diseases.

Finally, in order to evaluate the risks, cardiologists need to have an understanding of the different parameters used to express the degree of radiation that the patient is exposed to. In particular, the fluoroscopic time measures the total time that fluoroscopy is used but, if considered alone, this is likely to underestimate the exposure because it does not take into account the acquisitions. The cumulative air kerma (Grays) measures the dose at a particular spot and is closely linked with the risk of harmful tissue reactions. The dose area product (DAP) is the sum of the air kerma and the field of exposure. This provides a good estimate of the patient burden and provides an indication of the risk of stochastic effects. Risks for the staff must be considered also.

III. Methodology

In order to cover in the best way all main issues identified as above, a panel of experts was established for task 3.3 which worked together with external members according to the

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subspecialities identified (Non-invasive imaging – nuclear cardiology, cardiac CT, cardiac magnetic resonance) and invasive imaging (cath lab, electrophysiology lab) (M2-M3).

In particular, the following experts were involved in Task 3.3:

Task 3.3 Panel composition

Fondazione Toscana Gabriele Monasterio	Alessia Gimelli (AG)
Ludwig-Maximilians-Universität München	Joerg Hausleiter (JH)
COCIR	Riccardo Corridori (RC)
Hôpital Pitié-Salpêtrière	Alban Redheuil (AR)
University Hospital Zurich, Department of Nuclear Medicine,	Ronny Buechel (RB)
Royal Brompton & Harefield NHS Foundation Trust	Sabine Ernst (SE)
Leiden University Medical Center, The Netherlands, Department of Cardiology	Nina Ajmone Marsan (NAM)

Online meetings were held with the partners in order to define clinical subspecialties needed (M3-M6).

The open web-based survey proposed by the leadership of WP3 was filled in by Task 3.3 members in order to compile a list of clinical scenarios relevant to the aims of the task (M6)

In a first round of meeting, the experts proposed several suggestions to be evaluated and eventually implemented in the part of the SRA on applications of ionizing radiation for cardiovascular diseases:

1. Educational and research programmes related to the use of active dosimeters in the EP lab or cath lab
2. Use of artificial intelligence in advanced images
3. Use of CT as Anatomical approach for particular cardiac disease (GUCH)
4. Implementation of the use of imaging in the pre-procedural phase
5. Creation of an EU open platform for cardiac imaging data
6. Virtual reality and imaging

A shortlist of relevant clinical scenarios with related gaps of knowledge and needs of research and possibilities was also provided (See Annex 1).

In a follow up after the survey and based on a review of the published literature, all panel members and external experts agreed on the evaluation of the following main topics:

- Role of imaging in CAD prevention
- Role of Molecular Imaging and new tracers
- Cost Effectiveness
- Virtual reality

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- Artificial Intelligence

The above-mentioned shortlist of relevant clinical scenarios with related gaps of knowledge and needs of research and possibilities was updated and circulated among Task 3.3 members and a final consensus was obtained. Such different clinical scenarios and the related gaps in knowledge and need of research were presented to other relevant stakeholders at the European Radiation Protection Week Conference, held online in November 2021, for further discussion. The relevant suggestions and criticism were implemented in a consensus draft.

IV. Results & outcomes

IV a. Results

Cardiac Computed Tomography

State-of-the-art cardiac CT scanners are equipped with 64 or more detector rows. Several technological advances can and should be used to acquire cardiac CT data sets at low radiation doses.

The current PROTECTION VI data demonstrates that the radiation exposure from cardiac CT has been considerably reduced over the last 10 years by almost 80% (21). Greater use of reduced radiation tube currents and increased availability of statistical algorithms built into contemporary imaging devices were the main drivers of the decrease. According to the PROTECTION VI, independent predictors of increased radiation dose were an increase in body weight of 10 kg, an increase in heart rate of 10 bpm, and the absence of sinus rhythm. Additionally, compared with the axial scan technique, low-pitch helical scan mode was associated with a 313% increase in radiation dose, while use of the ECG-triggered high-pitch scan technique was associated with a nonsignificant 30% dose reduction.

Recent documents aim to provide a summary of the current evidence and to give indications on the appropriate use of cardiac CT in different clinical scenarios. Two comprehensive reviews on available strategies for radiation dose reduction in cardiac CT were published by EACVI, the Cardiovascular Committee of European Association of Nuclear Medicine, and the European Society of Cardiovascular Radiology in 2018, and, in 2011, the Society of Cardiovascular CT (SCCT) published dedicated guideline on radiation dose (5, 6, 22).

Accordingly, all these data can be used to reinforce the necessity to evaluate the state of the art of the EU technology and to plan a strategic road map to update hardware and software to reduce radiation dose.

Nuclear cardiology

Over the past 40 years, radionuclide myocardial perfusion imaging (MPI) has become a major tool in the non-invasive evaluation of CAD. During that time, advances in MPI technology and radiotracers have increased opportunities for improved diagnosis and treatment of patients with CAD.

Multiple professional societies have jointly developed appropriate use criteria to encourage the appropriate use of MPI and to lower the radiation dose from MPI. Manufacturers

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of nuclear medicine equipment have also responded to radiation concerns by introducing technologic advances that allow individualised low-dose protocols while maintaining or enhancing image quality, thereby paving the way for important changes in the practice of MPI. A growing number of nuclear medicine departments in Europe are now using a new generation of gamma cameras for cardiac imaging (8,9).

In these so-called 'CZT cameras', the conventional sodium/iodine (Na/I) crystal used for the detection of gamma rays has been replaced by a cadmium–zinc–telluride (CZT) crystal. The CZT gamma cameras provide a four- to seven-fold higher system sensitivity compared with Na/I-based cameras. This increase in signal detection efficiency has translated into a significant decrease in the dose of radiotracer required for cardiac scintigraphy. Another significant evolution has been provided by new reconstruction algorithms. Novel iterative reconstruction methods with resolution recovery and noise reduction provide higher image contrast (with sharper defects and borders) and significantly improve image quality, particularly for low-count imaging studies from half and quarter-dose radiotracer protocols (9).

Further technology developments and the use of artificial intelligence algorithm can provide new strategy to reduce radiation burden maintaining or increasing diagnostic and prognostic accuracy.

PET

Molecular imaging refers to the visualisation, characterisation and measurement of biological tissues at the molecular and cellular level. It can provide significant information regarding the underlying cellular and molecular mechanisms involved in various cardiovascular conditions. In the present era of precision medicine, molecular imaging is expected to play an increasingly important role in establishing clinical diagnoses as well as differentiating active from quiescent disease states, accelerating the development of novel drug therapies, and facilitating a personalised medicine approach where the right medication is targeted to the right patient at the right time. Indeed, molecular nuclear imaging is already being used in routine clinical practice. 18F-Fluorodeoxyglucose ([18F] FDG) PET imaging is recommended in clinical guidelines for the assessment of myocardial viability and in patients with suspected prosthetic valve endocarditis, cardiac sarcoidosis, and large vessel vasculitis. However, with the advent of improved PET scanners, sophisticated image analysis software and novel radiopharmaceuticals, there is major potential for these advanced imaging techniques to assume an even greater role in both the clinical and research domains. Further developments might be feasible with high spatial and or temporal resolution molecular imaging.

An ideal (radio-)tracer should have high specificity for its molecular target of interest (e.g., an enzyme, receptor, or transport protein) that is associated with a particular cell population or disease state with minimal off-target uptake in other tissues or cells. The tracer should also be robust, demonstrating stability during imaging and withstanding enzymatic degradation. Other qualities include prompt uptake into the tissues of interest, coupled with rapid clearance to facilitate high signal-to-noise ratios in the images. Whilst no radiotracer is perfect, several novel tracers demonstrate excellent imaging properties and now allow the in-vivo assessment of many of the key pathological processes underpinning cardiovascular disease, including inflammation, infection, calcification, fibrosis and thrombosis. Recent literature focused on the use of molecular imaging for the evaluation of viability, inflammation, atherosclerosis, sarcoidosis, innervation, infection, calcification and the results seem promised, even if more robust studies should be performed (23-30). Further developments are of great interest to improve molecular imaging for cardiovascular disease treatment further.

Invasive coronary angiography

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The use of ionising radiation has become central to the modern management of patients, in particular those with a range of cardiovascular conditions. It is therefore critical that cardiologists understand the risks and have strategies for reducing the dose. Educational program should be performed routinely, to implement the safety for the patients.

However, it is not just patients who are exposed to ionising radiation; cardiologists and the cardiac catheterisation laboratory team are also exposed during procedures (30-38).

A number of software and hardware developments have allowed a reduction in the dose received by the patient without altering the quality of the imaging. The use of different angulations during a procedure means that the radiation is spread over a wider area of skin thus reducing the risk of skin reactions. Furthermore, using less steep angulation during the procedure will also reduce the dose. Another simple way of reducing the dose is by reducing the imaging time or the field of view using collimation. Whilst all of these strategies will help reduce the dose received by the patient, it is important to balance this against the need to ensure the images are of sufficient quality to facilitate the procedure. An even better approach seems to be to acquire for the shortest possible time to allow diagnosis and then review the acquisition afterwards when no radiation is being used. The introduction of real time radiation dose feedback during procedures can help foster good procedural habits.

It is important to consider both the stochastic effects as well as harmful tissue reactions of ionising radiation to staff, also. Cataract formation commonly results from exposure and has been documented in up to 50% of interventional cardiologists. This is assumed to be a harmful tissue reaction and importantly the dose found to precipitate this has recently been reduced by a factor of 10. Skin and hair changes are often found as a harmful tissue reaction in interventional cardiologists. Vascular disease (macrovascular and microvascular) has been reported as a complication of radiation therapy, however the occupational significance remains unclear.

The main concern for clinical staff is the risk of neoplastic disease which is stochastic in nature. Studying this risk is difficult due to the long latency period which makes it difficult to attribute causation and also the challenge in identifying the additional risk attributable to the radiation exposure above the natural background exposure. All published studies are discrepant as to whether occupational radiation exposure is associated with an increase in neoplastic disease or cause mortality.

Despite the technological advances in the use of radiation in the cardiac catheterisation laboratory, there is still a clear risk associated with its use to both patients and the clinical team. Reducing the dose utilised in procedures should be a core skill for all cardiologists and there are a range of simple strategies that can reduce the risk to both staff and patients (30-38).

Key Points

- Persisting lack of standardization in the choice of imaging modality and acquisition protocols among different centers. The EURECA registry demonstrated how the adoption of the ESC GL is still reduced, and that the lack of adherence to the GL algorithm can increase the number of not necessary invasive procedure and thus of radiation dose. Moreover, the same registry seems to indicate the dis-homogeneous use of the state of the art algorithm for each procedure, with higher dose that expected in all the procedures.
- The knowledge about cumulative exposure dose due to diagnostic imaging from diagnosis to prognosis is limited. Cumulative dose can be very high, thus it could be very important monitoring

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- The knowledge about appropriateness and effectiveness of diagnostic imaging - with related dose exposure - during follow up is limited. More data on the real impact in terms of efficacy of each technique, as well as the best diagnostic and prognostic algorithm for each patient can change clinical decision making. The analysis of existing registry and trials could represent the starting point for the creation of different EU databases to be used for implementing the indication to reduce radiation dose.
- Further research on the opportunity offered by new (radio-)tracers for molecular cardiology is needed

IV b. Outcomes

a. Role of imaging in CAD prevention

Despite of the huge number of published papers, the absence of clear randomization of enrolled patients limited the outcome in terms of real changes of clinical practice. In particular, the difficult choice between anatomical or functional tests is due to a lack of adequately-designed prospective, randomised, outcome studies (20). Moreover, the prevalence of classical obstructive CAD (on which existing predictive models are based) is progressively decreasing in current populations referred to cardiac imaging for suspected CAD. In fact, the diffusion of preventive therapies, including the increased prevalence of statin treatment, have greatly reshaped CAD (39).

As part of the approach to primary prevention of cardiovascular disease (CVD), adults should have their CVD risk estimated using a population-appropriate risk equation. In the United States, the atherosclerotic cardiovascular disease (ASCVD) pooled cohort equations are recommended by the American College of Cardiology/American Heart Association (ACC/AHA) to estimate risk in patients ages 40 to 79 years. Accordingly, the estimation of risk can change the clinical decision making. In some situations, use of CVD risk enhancers, particularly coronary artery calcium assessed by computed tomography, may help inform the clinician-patient discussion.

According to these preliminary evaluations, the T3.3 agreed that there is a need for more robust research in the field of CVD prevention. In particular, it could be of great interest to create an international database for the evaluation of patients submitted to imaging for other disease (lung diseases, breast disease, etc). The use of big database/big data will allow the use of a machine learning approaches that can be of help in clinical practice to reduce not only the radiation dose, but also the burden of cardiovascular disease.

On the other side, the creation of big database of patients submitted to cardiac imaging for the evaluation of ischemic heart disease, valvular heart disease, aortic disease, could be of help to analyse the presence of different disease (breast diseases, lung disease...). As previously indicated, the possibility to centralise big data, will allow to use artificial intelligence for health care prevention.

Need for research:

- Prevention of CAD in patients submitted to imaging for other diseases: it would be of great importance to create a big database for the evaluation of patients

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- Prevention of other disease in patients submitted to imaging for evaluation of CAD
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b. Cost-effectiveness

The recent DANCAVAS Study assesses the cost effectiveness of screening vs. no screening from the perspective of European healthcare systems (40). Screening was based on: a) low-dose computed tomography to detect coronary artery calcification and aortic/iliac aneurysms, b) limb blood pressure measurements to detect peripheral artery disease and hypertension, c) telemetric assessment of the heart rhythm to detect atrial fibrillation, and d) measurements of the cholesterol and HgbA1c levels to detect metabolic diseases. Censoring-adjusted incremental costs, life years (LY), and quality-adjusted LY (QALY) were estimated and used for cost-effectiveness analysis. Assessing the population heterogeneity and evaluating the obtained results indicated that cost effectiveness could be more attractive for younger men without CVD at baseline.

According to the previous point (Role of imaging in CAD prevention), the use of big data can be of help to reduce the costs according to a prevention strategy.

On the other side, it could be of great importance to establish the role of radiation dose in the evaluation of patients with known or suspected CAD, according to the adherence in the clinical management as indicated by the current ESC Guidelines (20). To this purpose, the use of the EURECA data, after their exploitation, can open the door to a new research strategy for reducing the cost-effectiveness caused by radiation exposure. In fact, the evaluation of the real impact of the adoption of the current GL, can be of help to understand if the adherence to the "best" diagnostic and prognostic algorithm to reduce invasive and non-invasive not-indicated exams.

Need for research:

- The impact of radiation exposure and safety was discussed in this part, but, up to now, no dedicated research was performed in order to evaluate the impact of radiation exposure on cost-effectiveness. This is a very important gap in terms of research and could open the door on a new scenario: from the optimization of the workflow to the sustainability of the process to the efficacy for the patients.

c. Molecular Imaging

Advances in hybrid imaging technologies like PET-CT and PET/MRI alongside improved image analysis techniques allows the non-invasive assessment of disease activity in the heart as a clinical reality meanwhile. Whilst the lack of specific radiotracers was previously an important barrier, we now have an array of new tracers allowing us to measure inflammation, infection, fibrosis activity, calcification activity, myocardial sympathetic activity (cardiac innervation imaging) and thrombus formation as it is occurring in the body, potentially heralding a new era of cardiovascular imaging. However, despite its numerous benefits molecular imaging remains expensive and not readily available at all centres. The increasing use of PET to assess patients with cancer is gradually addressing both these issues but further collaborative work is required to make molecular imaging more accessible and equitable for patients. Future clinical studies will need to demonstrate the clinical utility and cost effectiveness of molecular imaging to justify its increased clinical use. In addition, there are still limitations in terms of spatial and temporal resolution parameters.

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The future of molecular cardiovascular imaging will also see a radical shift towards the use of artificial intelligence and machine learning platforms. Machine learning algorithms can efficiently connect information from multiple complex data sets and are therefore well suited to hybrid imaging where information from PET can be combined with the anatomical information provided by CT and MR.

Need for research:

- Precision-based medicine, defined as tailored therapy based on an individual's underlying disease biology, now underpins research and clinical aspirations within many medical specialities. Molecular imaging has the potential to deliver this potential by identifying the active processes driving cardiovascular disease in particular patients, which could then be targeted in a more precise manner. In addition, molecular assessments of disease activity are increasingly used as endpoint in clinical trials of novel therapy, providing rapid readouts that might accelerate the development of new treatments.
- To this purpose, the use of the new PET tracers or tracers potentially be used for other molecular imaging methods based on ionizing radiation technologies for the evaluation of inflammation and infection, viability, calcification, infiltrative disease, fibrosis, thrombosis or innervation, will play a pivotal role in improving our understanding of disease mechanisms, developing novel therapeutics as well as playing an increasing clinical role.

d. Virtual reality

The interest on the use of virtual reality in increasing, especially in cardiac practice and before the cardiac intervention. Integration of virtual reality with an algorithm model to provide integration of imaging data before cardiac intervention could be a relevant next step for cardiologists performing such therapeutic applications.

Need for research

- Impact of virtual reality on diagnosis and prognosis: how virtual reality can be of help to implement the accuracy of the diagnostic algorithm.
- Virtual reality for hybrid imaging in different kinds of disease: The use of virtual reality to merge different kind of anatomical and functional information to implement clinical decision making
- Virtual reality, imaging and interventional cardiologist. Impact of treatment and follow up: The use of virtual reality during invasive or surgical procedure to increase the efficacy of the procedure
- Potential role of virtual reality for education and training. Virtual reality can be used to implement the educational tools, creating a parallel and safety environment from basic to advanced learning.

e. Cardiac Magnetic Resonance

Cardiac magnetic resonance can be used for the evaluation of tissue characterization and functional analysis. It's use for the anatomical evaluation is actually more limited (CT is the gold standard for the evaluation of valve disease and coronary anatomy). However, the envelope of new technology and software reconstruction can be able to increase the accuracy in the anatomical evaluation, that in the past was promising.

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Moreover, new data should be collected on the possible side effects of CMR, due to its possible impact on immediate blood cell alterations or activations figuring inflammatory response, as well as DNA damage in T lymphocytes observed from day 2 until the first month but disappearing at 1-year follow-up. More results should be detailed to clarify this preliminary result.

V. Conclusions & recommendations

Cardiac imaging plays an important role in cardiovascular disease. Due to this point, there is the need to build an international network to implement the optimization on the use of imaging for reducing the burden of cardiovascular disease. Reduction in radiation dose exposure will be one of the main targets to reach, not only for patients, but for all the operators also. For the T 3.3 panel, the discussed points should characterise the main objectives of the strategic road map agenda for the expectations in CVD of ionising radiation and radiation protection.

To summarize:

- **a. Role of imaging in CAD prevention**
- **b. Cost-effectiveness**
- **c. Molecular Imaging**
- **d. Virtual reality**
- **e. Cardiac Magnetic Resonance**

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Annex 1

First Working Document

WP3 – Task 3.3

This on-going document collects and expands the subjects discussed in the meetings as well as other topics that arise during other meetings of the rocc-n-Roll project.

1st meeting: April 19, 2021.

2nd meeting: May 5, 2021

The current members of the panel, institutions and engagement in EURAMED rocc-n-roll are as follows:

Name	*Institution*	*rocc-n-roll*
Alessia Gimelli	FTGM	Task leader
Joerg Hausleiter	LMU	Task 3.3
Sabine Ernst		Task 3.3
Nina Ajmone Marsan		Task 3.3
Riccardo Corridori	COCIR	Task 3.3
Ronny Buechel		Task 3.3
Alban Redheuil		Task 3.3

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Short Task description:

Task 3.3 will analyse the needs of research in applying ionising radiation and the related radiation protection in cardiovascular diseases by identifying gaps and possibilities following the methodology of Tasks 3.1 and 3.2.

Relevant deliverable: D3.3 Medical application of ionising radiation and radiation protection in cardiovascular diseases (FTGM), (Draft in M25 and final version after 2nd workshop in M29), PU)

Original description in the Proposal:

Task 3.3 - Radiation application in cardiovascular diseases: needs and opportunities (FTGM; LMU,UPDescartes, COCIR; M2-M33)

Task 3.3 will analyse the needs of research in applying ionising radiation and the related radiation protection in cardiovascular diseases by identifying gaps and possibilities following the methodology of tasks 3.1 and 3.2. In addition, clinical situations in which the application of ionising radiation could be reduced or avoided in future in view of new scientific and technological developments will be analysed.

Next steps

- **Reorganise structure of this WORKING DOCUMENT - Three categories**
  - **Need for research**
  - **Need for action**
  - **Need for other things (legislation)**
- Relevant milestone MS7 by the UoC due on month 6 (February 2021) –
- **Include your thoughts in this document –**

Possible further steps:

- **Get input from COCIR**

Classification of topics

All topics should answer the question: **Where do we need research?**

Radiation in cardiology

The question for our group is **which research is required or expected from the experts in the different fields to cover gaps in radiation protection and to implement radiation** protection.

1. **Identification of different application of radiation in cardiac disease**
   1.1. Cardiac/Cardiovascular CT
   1.2. Nuclear cardiology
   1.3. Invasive cardiac imaging (cath lab)
   1.4. Electrophysiology
   1.5. Magnetic Resonance: despite the MRI is a non-ionising radiation, the diffusion of 3T and >3T equipment might introduce new problems and possible side effects. There are

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quite some contradicting literature, and – importantly- we need a call for action in order to evaluate adverse biologic effects of clinical MR imaging from the WHO and the ICNIRP. See ref below.

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From the IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. IARC Monogr Eval Carcinog Risks Hum 2002;80:1–395.

2. Technical Guidelines

2.1. Clinical Role of different imaging technique:

2.1.1. clinical indication

2.1.2. appropriateness criteria (Ref to the American Society of Cardiol)

2.2. Technical guidelines

2.2.1. Optimization protocol (see 2.1.1.) and also careful assessment of technology specific optimization (scanner generation, specific technical features,…)

2.2.2. Acquisition and data processing for diagnostic reference levels

2.2.3. Settings;

2.2.3.1. e.g. small spoke Hospitals vs. large multispecialty Hospital vs. Ultra-specialised CVS centers,…

2.2.3.2. remote-consultation with experts and also remote “piloting” of scans by expert operators (Techs and Cardiac Radiologist…)

3. State of the art of radiation dose

3.1. Literature analysis

3.2. Evaluation of quality assurance programs on radiation dose parameters in cardiology in the EU Countries (questionnaire?) (i.e.: In Germany, a federal quality assurance program is mandatory. Thus, a large scale German data on invasive procedures, but also TAVR, pacemaker etc are available)
Germany has a surveillance programme on Nuclear Cardiology, led by Oliver Lindner (https://pubmed.ncbi.nlm.nih.gov/31648359/). Plan is to have Switzerland on board as well as Austria in the next survey.

3.3. The concept of *diagnostic reference levels* for different cardiology procedures could be introduced. DRL are usually set a the 75th percentile of a large representative population. The values for CT and nuclear (from PROTECTION VI and Andrew Einsteins EHJ manuscript/INCAPS) are available. This concept could be introduced and reinforced within EU countries, because it might help to reduce dose over time.

4. Evaluation of new data results

4.1. EURECA (EUROPEAN REGISTRY ON CARDIOVASCULAR IMAGING) is an international registry proposed by the European Association of CardioVascular Imaging

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(EACVI). The aim of the registry is to evaluate the use of non-invasive cardiac imaging in a contemporary large population of patients with stable symptoms potentially caused by underlying obstructive CAD. The radiation dose for each modality in each enrolled patient is requested. The main purpose is to fill the gap of knowledge on the real-world practice in this population. The factors conditioning adherence to Guidelines, local variability in the use of different modalities and possible effects on patient management will be assessed.
Analysis of the EURECA data about the mean radiation dose in different centres in EU for imaging techniques
Comparison between clinical practice (EURECA) and optimised protocol: fill the gaps

4.2 Data on cath lab (do we have a new one)

4.3 Data on EP studies

4.4 Data on cardiac CT: Will be available with INCAPS2 study, that was postponed due to COVID-19

4.5 Data on pediatric pts: The EPI-CT study may provide important information. Over 1 Mio pediatric patients. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6469297/ . Furthermore, a new EU consensus statement between the different cardiological associations will be published up to the end of the year

Role of imaging in prevention

Need for research:

- Prevention of CAD in pts submitted to imaging for other disease
- Prevention of other disease in pts submitted to imaging for evaluation of CAD

Need for action: OPEN ACCESS Platform and AI

- One of the main research areas could be related to the creation of an European OPEN ACCESS platform for cardiac imaging. The open access platform will be the first step for several different research questions, starting from creation of dedicated EU database.
- Tips and tricks of different kind of acquisition and evaluation of optimization protocols
- Computer – assisted diagnosis → optimization of protocols and of the workflow. This process could allow the use of complex tools everywhere, with the possibility to reduce the costs and increase the sustainability of the diagnosis of cardiac diseases that still represent one of the major causes of mortality in the world.

Cost-effectiveness

Need for research:

- The impact of radiation dose and safety was discussed in the part, but, up to now, no dedicated research was performed in order to evaluate the impact of radiation dose on cost-effectiveness. This is a very important gap in terms of research and could

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open the door on a new scenario: from the optimization of the workflow to the sustainability of the process to the efficacy for the pts.

Need for action:

- Integration of radiation dose in the workflow of pts with CAD (patients and physicians)
- Evaluation of costs
- Evaluation of cost effectiveness including radiation dose
- Cost effectiveness and radiation protection for screening. Tips and tricks of Prevention and Radiation dose → Grey zone of the GuideLines
- Cost effectiveness procedures to justify imaging procedures in the process of individual health assessment

Virtual reality

Need for research

- Impact of virtual reality on diagnosis and prognosis.
- Virtual reality for hybrid imaging in different kind of disease
- Virtual reality, imaging and interventional cardiologist. Impact of treatment and follow up

Need for action

- Integration of virtual reality with an algorithm model to provide integration of imaging data before cardiac intervention and possible outcome

Operators and radiation dose protection→ To be connected with other TFs

Need for action

I.E.: In the cath lab or in the EP lab: First operator gets the most of radiation and he/she's the only person who can guide the procedure.

- Education
- Provide ACTIVE DOSIMETER to physicians to reduce exposure.
- Education and training of staff
- Internal and external audits
- Legislation
-

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