

Supplemental Appendix– CMR vs SPECT for the diagnosis of stable CAD

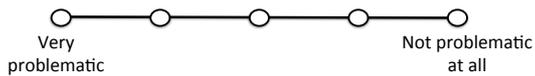
Table of content

Questionnaire submitted to the nine Swiss hospitals 2
Interview with Expert 1 (Nuclear Medicine specialist), Hospital 1 4
Interview with Expert 2 (Cardiologist), Hospital 2 7

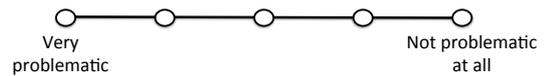
Questionnaire submitted to the nine Swiss hospitals

1. Name of your hospital:
2. Domain of activity: (Cardiologist, MRI specialist, Radiologist, Administration)
3. Hierarchical level : (Assistentarzt, Oberarzt, Chefarzt, Klinikdirektor, Other)
4. In your opinion, what are the main problems associated with the use of SPECT or cMRI for the diagnosis of stable coronary artery disease (CAD):
 - a. **Availability or access** to the MRI or SPECT **machines** (eg. booked for other diagnostics, insufficient technical personal) is:

For MRI machines

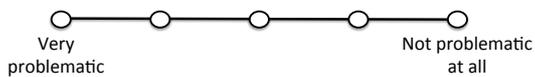


For SPECT machines

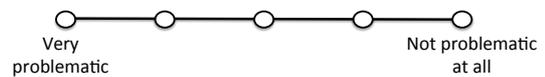


- b. **Time and effort** required for the examination is:

For cMRI

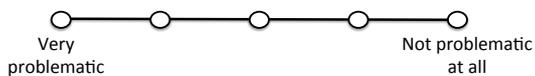


For SPECT

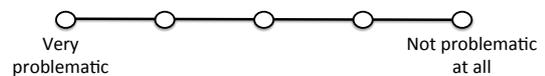


- c. The **contra-indications** of the techniques for their implementation in the diagnosis of CAD are:

For cMRI

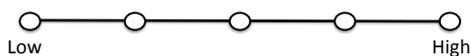


For SPECT

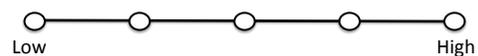


- d. The **initial diagnostic** cost is :

For cMRI

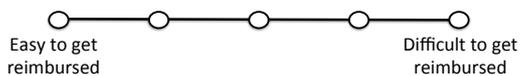


For SPECT

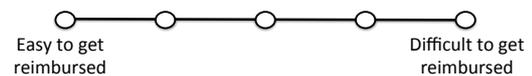


- e. The willingness of the insurance to **reimburse** is:

For cMRI

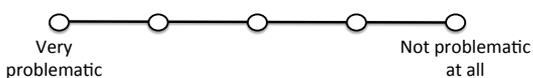


For SPECT

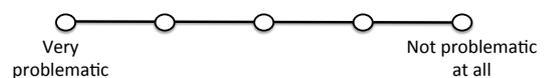


- f. The **availability of the corresponding specialists** for the interpretation of the result is:

For cMRI

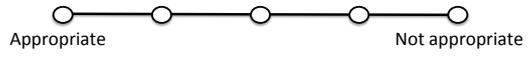


For SPECT

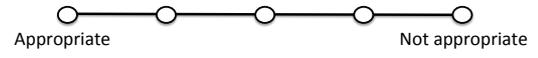


g. For the **diagnostic** of stable coronary artery disease, these non-invasive techniques are:

cMRI



SPECT



Interview with Expert 1 (Nuclear Medicine specialist), Hospital 1

How do you perceive the implementation of CMR and SPECT for the diagnosis of stable CAD in your hospital?

Already on the level of the patients referral we can observe differences, especially here in our hospital. The SPECT exists here for a much longer time than the CMR does. Since the very first balloon dilatation was conducted here, all procedures were preceded with a SPECT. The professor in charge at this time said a functional imaging was necessary before such an intervention. Since his time here, the SPECT became a sort of tradition. When the CMR arrived in the hospital, it has been seen as a very promising technology and that this new technology would maybe even replace the CAG and perfectly demonstrate the anatomy of the coronary arteries. The cardiologists here are definitively believers of this technology and the SPECT slowly lost in importance over the years. I also believed CMR was a promising technology, but in the meantime, other technologies made much quicker progress, like the CT, which can now insure a good anatomic representation of the coronary arteries. I believe CMR will not become the leading technology for the diagnosis of stable CAD. If there should be one, then it will be the PET-CT, clearly.

You mentioned differences on the level of patients' referral, what do you mean?

In the past, we got a lot of patients referred for SPECT and for PET-CT. Today, due to structural modifications a lot of patients are preferably referred for CMR over SPECT. These "structural" modifications are for instance the presence of a senior physician working on the cardiology ward but also salaried by the radiology who strongly believes in the CMR technology. The cardiology department of course is glad to see its CMRs numbers growing and further promote this development.

There are also further conflicts of interest in our structure. For instance, we have an institute of biomedical technologies and a polytechnic university next door, and the use of CMR in the research to improve the characterization of perfusion is of primary importance for this institute. As the CMR does not imply any ionizing radiation, physicists without license for radiation protection can proceed to studies with a consequent numbers of subjects or patients. These patients are not exposed to any ionizing radiation, this also allows for a higher number of participants. This is a handy technology to study, and there where research is conducted, the industry also has its own interests in these developments.

In our hospital, a cardiac MR is available on the nuclear medicine ward and on the cardiology ward. On our ward, our numbers for the CMR stayed quite constant over the last years, while there seem to be some interests on the cardiology ward to see these numbers growing. I also believe the CMR is a good technology, but the referrals should be driven by patients characteristics, current available data and local availability, but not by the financial interests of the departments. Here on the nuclear medicine, we have no personal advantage or disadvantage if we use an imaging method over another. In Basel, the system is quite similar, they do not get any personal benefit out of one or the other method. In Lausanne however, the chief of the cardiology ward is an expert in CMR and cardiologists have there the possibility to conduct and bill CMR on the radiology ward. Therefore, the number of CMR conducted in Lausanne is so high, and the number of SPECT so low. Again in Geneva, the numbers are the other way round: they conduct much more SPECT and much less CMR. In Ticino or in St. Gallen, I can imagine the numbers are quite similar, with a small preference for SPECT as this is a robust "working horse" for years. When the numbers of conducted interventions are so different across the country despite having the same European guidelines, there are clearly personal interests coming into play. I believe that there where the cardiologists are strongly

implicated and favor one technique, the numbers are not balanced anymore at all. And this technology is then always CMR, as it does not have any ionizing radiation for which a license would be required and as they can bill it on their own ward. It has been recently communicated by the FMH (Swiss Medical Association) that the CMR will become part of the trainings of cardiologists, who will also be allowed to charge for this intervention. In the future, we can expect them to favor the use of this technology even more. These conflicts of interests are enormously important. In the nuclear medicine, we are the receivers: We do not have any consultation hours and we do not send patients for further investigations, the cardiologists do, and if they decide they want to diagnose all their patients through their own techniques, they will.

And the availability of the scans is not a problem in your hospital?

The availability of the CMR scans or SPECT is absolutely not a problem here. We are extremely well equipped and should the number of patients increase and our capacity limited, we would instantaneously react by first increasing personal and working hours, and then probably buy a new scan. We also have to take in account that we are in competition with private diagnostic institutes, which can react very quickly as well and would buy a new scan right away. To stay competitive, we have to monitor our numbers tightly and having an actualized business plan. The availability of PET is much more problematic. The use of the isotopes is much more complicated than the use of gadolinium for CMR and their generation is expensive if the number of investigations per day is low. A private diagnostic institute will never buy such a generator and despite the PET being a better technology as they would not have the required number of patients to make profit.

How do you see the future evolution of these technologies?

It is extremely difficult to predict the evolution of these technologies, but I believe the nuclear medicine will slowly get away from gamma-ray technologies to favor isotope-based technologies, such as the PET, which happens to be a very good technology. However, cardiologists are the “patients owners” and if they are motivated to charge more often for investigation they realized themselves, we have to expect a much higher growth on the CMR side. My former superior taught me “If you want to understand patients’ flow, you have to understand cash flows”. It is a reality and I believe this is the reason why we need to establish a way to control for patients referral. Otherwise, there were there is a separation of powers, the use of CMR and probably PET in the future will stay balanced, while there where the cardiologists can decide with which technology patients will be assessed, we will see a clear bias in favor of CMR. The radiology and cardiology are usually consequent departments in many hospitals, while the nuclear medicine is small in most of the structures. Many cantons hospital and all university hospitals have consequents cardiology departments and these personal interests together with the size of the departments will probably lead to an always stronger bias in favor of CMR in the future.

When you look at the countries around, do you feel they live the same situation?

In the USA, the CMR for the diagnosis of stable CAD is still “off-label use”, partly due to the needed high dose of Gadolinium, which has not been approved by the FDA. We can ask ourselves why the FDA has not approved these gadolinium doses yet. I believe there is a safety reason, because it has never been shown to be safe, and a necessity reason as well : SPECT is working well for the diagnosis of stable CAD and they probably decided it was not worth it validating CMR for this use. I believe the USA will more go direction PET-CT, which is more accurate.

What do you think about the available literature regarding SPECT and CMR for the diagnosis of stable CAD?

In the CE-MARC I study, the CMR were conducted and interpreted by experts, while the SPECTs were read by, I believe, a PhD student. This is clearly not a valid comparison. Even in their article, they present some example data and the belonging interpretation, namely saying that the presented SPECT is a normal SPECT, while we can clearly see a defect. If we can see interpretations errors already in the data the present as examples, I don't want to imagine the rest.

Regarding the CE-MARC II study, I struggle with their first endpoint, namely the "unnecessary angiographies", which were higher for SPECT than CMR. SPECT was overruled more often than the CMR, meaning that the cardiologists thought that SPECT more often delivered a wrong result and decided to proceed to an angiography. This angiography then showed no disease, was classified as an "unnecessary" associated to SPECT, and distorted the results.

In the MR-IMPACT II study, they concluded to the inferiority of CMR versus SPECT already in the abstract. But all the subgroups analysis based and these data and published later, showed strong advantage of CMR versus SPECT, for patients with diabetes, multi-vessel diseases, women etc.... so that the author concluded in the end that CMR was better for the whole population.

There are further problems in the literature regarding the evaluation of CMR versus SPECT for the diagnosis of CAD and a thorough review of these studies let me suspicious of their conduction.

Interview with Expert 2 (Cardiologist), Hospital 2

What do you think of the use of CMR and SPECT for the diagnosis of stable CAD?

In the nuclear cardiology, we use SPECT or PET, the latter being especially good for the diagnosis of ischemia. Even if the CE-MARC or MR-IMPACT study showed excellent results of the CMR, it seems clear in the practice that PET combined with an angio-CT is nowadays the most sensitive way to diagnose ischemia. The CMR has totally different advantages, like the characterization of the myocardium where we can see if previous myocardial infarction took place. With the CMR the diagnosis of ischemia is possible but delicate, as influenced by extrasystoles, atrial fibrillation, differences in breathing or by patients who are not cooperative. The softwares used for the CMR are still much less performing than the ones used for SPECT, at least in the domain of ischemia diagnosis. The coronaries are not satisfactorily visible using CMR, while we can combine a SPECT or a PET with a CT to have a good representation. A PET-CT has then the big advantage to show us the coronary arteries : If they are normal a CAD is excluded. If they are not normal, the combined PET will show us the ischemia.

For patients in whom we are looking exclusively for the presence of a CAD and for whom we want to define whether or not the troubles come from the coronary arteries and to stratify the risk, we use nuclear cardiology methods. If we want to know where a reduced pump function comes from, we send the patients in CMR. The search for ischemia is then a small element but the myocardium characterization is there the central point. Both techniques are then complementary and will not be used in the same way for the same patients. This is also something that you need to take into consideration when looking at the numbers you collected. You collected the numbers of CMR for ischemia diagnosis only, but it is not rare that we look for ischemia in a CMR that we realize for another primary indication. I believe that for our hospital, we realized about 1000 CMR a year against 1600 SPECT. Not all the CMR are realized for ischemia diagnosis, but during about 250 CMR, we are looking for ischemic components and trying to elucidate unclear cardiac values.

Then, it is clear that both techniques have their disadvantages: We don't send a young 20-y patient in whom we are looking for a CAD to the nuclear medicine but will conduct a stress echocardiography, because we want to minimize the risks from the radiations. But with the PET, the radiation could now be heavily reduced. In the everyday life, only Zürich and Basel really realize PET.

I am a fan of the patients-centered approach where I look at what the patient need and then I look at which method gives me the best answer. But in this hospital I am in a luxurious situation when I don't win anything if I conduct a SPECT or a CMR. I decide based on what the patient needs and my decision is not biased by any possible financial gain, we don't have any here.

How do you see the evolution of these technologies in the future?

PET should be used instead of SPECT because it is much more sensitive and has less radiation. In the USA, where much more nuclear cardiology is done, there are some interesting developments showing that the PET is not taking as much importance as expected, as it is not possibly implementable in private practices or smaller hospitals, while a SPECT can still be implemented if the everyday use is a sufficient number of procedures are realized. It is difficult to estimate how it will evolve, but I don't think that CMR will become the technique of choice to diagnose stable CAD. The local expertise, preference and availability will stay the most important point regarding which technique will be used for which patient.

When you decide that a SPECT or a CMR will be conducted in a patient, does the price has an effect on your decision?

Well, prices are virtual and arbitrary. A drug or a procedure here in Switzerland can cost a multiple of what they pay next door in Germany, and sincerely, I don't see why. We have to follow the same European guidelines but the real comparison between countries is especially difficult. For instance, a coronary stent in Germany can be a third of the price of the same stent in Switzerland, the reasons why are not clear, at least not for the clinicians.

Then the question is what do I have as information for this price. If I do a CMR with everything included, it is going to cost about half to two-thirds of the price of a PET-CT. However, if I want information regarding the coronaries, I need to realize a CT following the CMR, which in the end, is going to be as expensive as the first combined technique.

The next question to ask is "What does an imaging technique tells me? What do I do with the results?". If I can already be sure to a high degree of certainty that the patient is free of CAD, it is efficiently invested money. The answer is clear, and there is no need for a succession of tests, for which the total cost will be much higher than one initial more expensive technique. The downstream costs are also difficult to take into consideration and there is a need for further research and more awareness in this field. If a patient has a normal coronary CT, a normal perfusion and no diabetes, I can be sure that there is a "guarantee" of 5 to 15 years. If during this time, the symptoms stay stable, no further ischemia diagnostic should be realized. A CMR or a SPECT without a CT or ergometry has a maximal "guarantee time" of two years, and in a diabetic even only one year. This is because they look only at the function, namely the perfusion, not at the coronary arteries. These are parameters that are central to take into account, but the current state of knowledge is still poor.

An economic evaluation requires a lot of assumptions, which are not the problem when they are derived from appropriate sources. However, during the conduction of these evaluations, a lot of factors are forgotten and not taken into account. The diagnosis of CAD and the related decisions of the clinician is extremely complex and when I look at the cost-evaluations that have been conducted in the past, important components are lacking.