PET/MR: A CLINICAL REALITY CHECK

An interview with Professor Gustav K. von Schulthess, MD, PhD, MD Hon, Chairman of the Department of Medical Radiology, Professor and Director of Nuclear Medicine, University Hospital, Zurich

How are you using the PET/CT + MR Tri-modality solution at Zurich University?
Eleven years ago, we were the first clinical PET/CT users in the world. At that time, there was PET and then PET/CT. We had a clinical need for the technology and the technology satisfied that need.

With PET/MR, it is a totally different situation. PET/MR as a technology is looking for an application. PET/CT for oncological questions is a very good modality, and so we are now in a situation where we have to demonstrate that integrated PET/MR is actually living up to the gold standard of PET/CT.

We are evaluating whether there are applications where PET/MR is comparable or better than PET/CT. Today with a carcinoma patient, I can’t evaluate them with just PET/MR, I also need to use PET/CT because I have not proven that some of the information I get from CT I will have on MR and, therefore, I could make a misdiagnosis. So we need to prove in large data sets, with hundreds of patients, that replacing PET/CT with PET/MR will not lead to a misdiagnosis. I want to replace something good with something better.

With our Tri-modality, we are doing a clinical PET/CT exam and a clinical or research MR exam. Every patient in our system has received a clinically relevant examination. An integrated PET/MR is a “sexy” system, but at this point it is not clinically validated. It may turn out that we miss 30% of the lung lesions if we only use PET/MR. If I can shift certain exams from PET/CT to PET/MR without compromising diagnostic accuracy, then I would buy a fully integrated system.

Figure 1. T2 and T1 images of the brain fused with PET demonstrate a recurrence of astrocytoma WHO grade II.

All mention/discussion of PET/MR and PET/MR images in this article refers to the PET and MR components of the Tri-modality solution installed at University Hospital, Zurich, and images obtained from that system.
So why not just compare an integrated PET/MR to validate against PET/CT versus using the Tri-modality solution? A set-up such as our Tri-modality is an excellent way to prove clinical usefulness, and it is likely a better set-up than a fully integrated system. With a fully integrated system, if we want to compare PET/CT with PET/MR, we have to take the patient off the PET/MR and onto PET/CT to compare two data sets. The problem is that the PET scanner in the PET/CT and the PET scanner in the PET/MR are different scanners, and you acquire the PET at two different times so the distribution of radioactive sugar differ somewhat. Therefore, comparing PET/CT and PET/MR in this way is not a very clean experiment, as multiple parameters have to be changed (CT->MR, PET Scanner 1->2, Sugar uptake time 1->2).

With the Tri-modality, we have one PET, one CT, and one MR examination. We shuttle the patient between the systems, and the MR is taken at a different time than the CT. However, we believe the issue of simultaneous imaging made possible with a fully integrated PET/MR system is rather a moot issue—we don’t really know what simultaneous means. For example, when we inject a contrast and wait one hour after the injection before scanning, then what is “simultaneous” when you acquire the data?

Figure 2. Note the fewer artifacts on the fused brain images in the PET/MR (left column) compared to the PET/CT (right column).
What have you learned thus far in terms of where PET/MR can make a difference?

Not unsurprisingly, PET/MR is better where MR is better. But we don’t have enough data yet to make strong conclusions. If I say MR is better than CT it doesn’t mean PET/MR is better than PET/CT. It may be that in all the aspects where CT is weak compared to MR that PET will actually jump in. If you see a lesion with PET/MR and with PET/CT, then you still see the lesion in the examination.

However, we know in the liver, abdomen, head and neck, and brain that PET/MR is probably equal or better than PET/CT. The most critical organ is the lung; most tumors make lung metastases, and if I do a whole body MR tumor search from head to toe, and the lung is the black hole for MR, we have a diagnostic problem. MR lung imaging is not good and I will miss some metastases using current techniques. So the question now is: Can we set up PET/MR pulse sequences so the lung does not appear as black? Other questions are: What percent of the lung lesions do we miss and, on the other hand, if we see more lesions in the brain, but less in the lung, what impact does that have on patient treatment? So, these are very important clinical issues that we must address.

The second thing we have learned—PET/CT is a synergistic modality, not only because CT provides anatomy and additional anatomic information but it also permits attenuation correction for PET. For a PET scan to provide quantitative data, we need to correct the self absorption of the gamma rays in the patient. CT data in essence provides such an attenuation map. MR data, on the other hand, have nothing to do with attenuation of ionizing radiation and cannot a priori be used for that purpose. Particularly, we don’t see bones well on MR, and there are no pulse sequences or other software/hardware that can consistently bring out the bones in a very meaningful way up to now.

If we use MR for attenuation correction, the only way we can do this is to ignore the bone or replace it with soft tissue. We have done a simulation on that—
we took the CT data and used the de-boned data for attenuation correction. For bone metastases, such “de-boned” scans are not good enough for quantifying. We underestimate the values by up to 25% and the underestimation is very inconsistent as it relies on whether the metastases are lytic or sclerotic. This will be a problem in therapy monitoring—bone metastases can change from being lytic to sclerotic and if we cannot correct for that, then we make mistakes determining whether a tumor is progressing or reacting to therapy.

Were there any issues you’ve encountered with setting up the Tri-modality solution?
We had to set up the transfer from PET/CT to MR, and while it went well, it took us quite some time. We have learned some technical and some clinical things, but now the system is ready to start to produce the amount of clinical data needed.

Can you share any initial clinical impressions?
I cannot make any clinical judgments yet, but I can say it is fairly clear that the way PET/MR is working today is insufficient for therapy monitoring of bone metastases. In lung imaging, there is hope, although I’m not certain existing pulse sequences will be sufficient. We looked at lung CT versus lung MR and found that, on a lesion-by-lesion basis, CT outperforms PET, and on a patient-by-patient basis, MR is close to CT. In essence, whether I see one or five lesions, it doesn’t make much difference. However, we don’t yet have the whole gestalt; for example, with melanoma cases, identifying brain metastases more readily than lung metastases may be an advantage.

So is a Tri-modality solution the way to go versus PET/CT or PET/MR?
I can’t answer yes or no at this point in time. We have not found a clinically relevant case where a fully integrated system is doing better than a separate system. The only positive aspect of the fully integrated solution may be that it is more comfortable for the patient as the overall imaging time is shorter then when a PET and an MR are done separately. Regarding PET/CT versus PET/MR, we know that a PET/CT doesn’t take longer than PET/MR. But it’s hard to say there is a major advantage of a fully integrated PET/MR from a clinical perspective, although there is interesting research that can be done. For those 4,000-plus institutions wondering whether they should have access to PET/MR without wanting to do more basic research, if they can shuttle the patient between the systems, then I believe they have a more flexible solution.

Why is that—a more flexible approach by shuttling the patient from one system to another?
In the morning, we conduct integrated PET/CT + MR studies and in the afternoon we perform separate MR and PET/CT studies. So the advantage here is you can use these systems individually for clinical exams; for example, we are doing standard MR sequences in the brain, MSK, and abdomen. Also, for PET/MR we can be very efficient. When patient #1 is undergoing PET/CT, patient #2 can also undergo an MR, and so on. Hence, the systems running multiple PET/CT and MR patients are almost utilized to their fullest capacity.

Is image fusion an issue when shuttling the patient?
It is easier to perform image fusion in the brain than other anatomic areas. We can do that with software—it is very easy to superimpose two brains in the proper way. In the brain, there is no
reason to have fully integrated imaging. That's the reason why PET/CT never took off in the brain; first, MR is better, and second, image fusion is easy. The integration and the hardware fusion most relevant is with whole body imaging. In the abdomen, organs and anatomy move around—the bladder fills, bowels shift—so in these studies the integrated similar time imaging makes more sense.

We already have years of experience that shuttling patients won’t cause issues with image fusion because all PET/CT systems shuttle the patient from CT to PET. So whether you shuttle the patient 60 cm or over 5 m, you don’t have an issue with a cooperative patient. Oncology patients are generally cooperative patients, as they are mostly not demented. This issue may be different in PET/MR of dementia patients.

As a clinician, I am interpreting images. So if I have a fused image that is 1 mm off, even 3 mm off, but I see an FDG activity focus on PET and the morphologic lesion on CT or MR, then I know these belong together. PET needs CT or MR to frame the image within the anatomy—PET is the pointer that tells me to look in a region within 2 cm around the PET focus. It helps me narrow down to a much smaller area where I need to examine the anatomy to find the lesion, compared to having no information from PET.

Is a Tri-modality solution more financially sustainable than an integrated system?

A few years ago, we published a paper that concluded a Tri-modality set-up would provide a patient pipeline. For example, if you examine 15 patients, you scan them first in the MR and then move them into the PET/CT. The MR is then free again to receive the next patient, so both systems can be running nearly all the time. With a
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University Hospital Zurich is one of the largest and most important teaching hospitals in Europe. With its 40 divisions and institutes, the hospital is renowned for its achievements in healthcare, research and teaching, as well as for compassionate care. It offers state-of-the-art treatment for a broad range of illnesses, provided by a dedicated team of leading consultants of the highest international standing.

In some major indications in oncology, because 95% of my PET/CT exams are for oncology.

However, we don’t know what the future holds, and it appears we’ll have a greater need for dementia imaging, which needs both PET and MR. Although we can perform PET and MR separately, there may be an advantage for the patient with an integrated system because we often have to sedate them. There is also the comfort issue we discussed. However, from a clinical standpoint, we can take care of the patient just as well with separate systems as with a fully integrated system.

So where do we need PET/MR?

Potentially in dementia; we haven’t proven its clinical value yet in oncology. PET/MR is a technology that is desperately looking for a good clinical application. I’m not saying integrated PET/MR isn’t an interesting technology, but MR will have to adapt to the pace of a PET acquisition to function along with it. I like to say, ‘The wild horse MR has to be tamed to trek along with the donkey of PET.’ With PET/CT, we had to learn how to run CT differently to conform to PET, and the same thing holds true with MR.

References