

Diagnostic neuroradiology: Ready for the neuro-interventional age?

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Abstract

Acute cerebral ischemia or stroke is currently considered an emergency for which therapeutic options are available if the therapeutic window of 4.5 h is respected. Imaging modalities have progressed greatly over the last few decades, rendering ischemia detectable in the first hours after the event. However, in order for treatment to be efficacious it is necessary to speed up all the processes before the start of therapy. Thus, one must decrease the time to arrival at the hospital and to the radiological method that is to be employed (be it computed tomography or magnetic resonance imaging); only then will the medical or interventional techniques available fulfill their potential.

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INVITED COMMENTARY ON HOT ARTICLES

Over the last twenty years enormous advances have been made in the clinical management of acute stroke: while before the 1990s stroke was considered a disease without any possible realistic therapeutic options being available, both from a diagnostic and therapeutic point of view great efforts have been made in parallel over the last two decades. Indeed, thrombolysis with recombinant tissue plasminogen activator within the therapeutic window of 4.5 h is now the accepted standard of care^[1]; imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI) that were previously poorly understood have now revealed themselves to be powerful tools for the detection of ischemia. However, as stated in a recent study by Kelly *et al*^[2], only 41% of patients are scanned within 25 minutes of emergency room arrival. This study once again shows that while much has been done to improve the technological quality of stroke management, there is still a lot to achieve when it comes to improving overall management and especially time management.

When considering ischemic stroke, there is a rather strict limitation due to the inherent sensitivity of the parenchyma to the decrease in blood flow: this very quickly will lead to necrosis if reperfusion does not occur. If reperfusion is not spontaneous, methods to induce it are available such as intravenous thrombolysis, intra-arterial thrombolysis or even mechanical thrombectomy^[3]; whatever therapeutic option is chosen, it must be done very

quickly. From a diagnostic point of view, a non-ischemic cause of stroke must be excluded, ischemia demonstrated and the vessel occlusion documented. This must thus be done in the rather strict therapeutic time window in which intervention will be possible.

The development of integrated stroke units with 24 h availability of a neurology team, along with specialized imaging and an intensive care unit, have improved outcomes and patient handling to a great degree.

In the domain of neuroradiology, parallel advances have been going on both in the interventional and diagnostic fields^[3-7]. MRI and CT are now able to visualize parenchyma, obtain perfusion images and visualize vessels with a degree of resolution that was unheard of until recently. CT remains more easy to use since it allows a more reliable detection of hemorrhage^[4], also CT angiography does provide a luminographic filling of the vessel that makes it comparable to digital subtraction angiography for the assessment of occluded vessels; in addition to perfusion imaging it becomes a very powerful tool. CT perfusion, which is often performed in the same session, has the advantage of being quickly available for the decision: thus, today this technique can reliably detect reduced perfusion as well as detect false negatives or positives. There have been great advances in the mapping capabilities of post-processing software so that one can obtain the necessary values of cerebral blood flow, cerebral blood volume, mean transit time and time-to-peak; initially only a few select slices were available and this required the technician and radiologist in charge to be certain to cover the area of interest. In order not to miss the less perfused area, newer scanners offer more and more coverage so that this should be no great problem. MR perfusion, as described below, has for a long time provided whole-brain coverage, which is a great advantage.

MRI in stroke was revolutionized by the clinical implementation of echo-planar sequences since these allowed us to obtain diffusion-weighted MR images^[8], perfusion images and fast T2* images^[5]. Diffusion weighted images allow the detection of early water redistribution in the brain and thus ultra-early detection of ischemia; in this it is a much more powerful tool than CT. Due to the higher inherent contrast of the diffusion weighted images, the technique also offers a better early delineation of the acute infarct which is of prime importance to assess the size, which will inevitably affect outcome^[8]. Perfusion imaging, which allows the assessment of any hemodynamic changes caused by the occlusion, is also of additional great help since it allowed investigators early on to formulate a working model of a potential penumbra. This hemodynamically-driven model of the penumbra, which defines a so-called mismatch zone between the areas of restricted diffusion and diminished perfusion (the diffusion-perfusion mismatch), does not actually correspond to the classic model of the penumbra where areas of electrical dysfunction secondary to reduced perfusion cause diminished neurological function that may be re-

versible. However, while not being perfect it has shown itself to be a model that can be used in part. With the implementation of real clinical high-field scanners, it has been also possible to make use of a technique such as arterial spin labeling (ASL) in patients^[9]. This technique, which does not use contrast, can be used to detect the presence of collateral blood flow in selected patients. Indeed, besides angiography and ultrasound techniques, most axial imaging methods have not been reliable for the detection of collateral or rest flow. This collateral flow is believed, and also proven, to provide hemodynamic support to the acutely ischemic tissue. Being able to demonstrate its presence reliably and quickly would be an enormous advance. Additionally, blood oxygen level dependent (BOLD) type imaging could be of interest for patients with a potentially salvageable penumbra; indeed, BOLD imaging is used principally for brain activation studies due to its capacity to demonstrate blood oxygenation differences. It is believed that this advantage could be used with success in the border of the infarcted area, since there should be a compensatory increased extraction of oxygen in this border area^[10]. This imaging technique has until now, however, found less popular acceptance than ASL or standard perfusion techniques, mainly due to issues with more complex post-processing.

Also and almost in parallel, the field of interventional neuroradiology has experienced continuous developments with adaptations of devices that now allow not just intra-arterial thrombolysis, but also thrombectomy with increasingly improved results. Indeed, while initially local thrombolysis was performed, more and more studies have demonstrated the feasibility of thrombus removal by mechanical means, be it aspiration or more advanced techniques such as using the MERCI device. Recently, an emphasis has been put on the use of temporary devices such as removable stents or “stentriev-ers” (i.e., stents with a clot retriever function)^[3]. These stentriev-ers have the advantage of recanalization offered by the stent on the one hand and of clot removal by the retrieval system on the other hand.

While all these evolutions have improved our handling of these cases, they have not yet led to the expected revolution: except for selected high-technology centers, stroke remains unfortunately a disease where management still has to be improved upon. Sometimes, even in highly equipped centers, only 10% of patients referred for stroke will undergo treatment. While many factors such as late arrival can only be addressed by public campaigns in order to heighten awareness of the disease as a treatable entity, there are some other in-hospital factors that need to be changed in order for the management to be optimized.

One important point is that imaging should help and not interfere with treatment: it has to be available quickly and be done quickly. One problem with the very advanced CT and MR techniques is that they allow us to provide very often complex answers in situations that are acute and require a rapid decision. In such situations

it is necessary to have people that are experienced in the reading and interpretation of acute CT signs and in the various perfusion parametric maps. It is thus necessary to have specialized diagnostic neuroradiologists present in the emergency room for when imaging is done.

Transport by ambulance seems to improve time reduction, which is obvious since the transport may help to immediately direct the patient to the stroke unit. Subsequent handling by specialized emergency care physicians who are well aware of stroke as an emergency seems of prime importance.

Once in the hospital, it is also important to go as quickly as possible to imaging. Indeed, the first thing to do in any situation when confronted with a stroke is to exclude another pathology: the most important pathology to exclude remains, of course, hemorrhage since thrombolysis cannot be performed if there has been acute bleeding.

In order to obtain the maximum information, many investigators have promoted the so-called “one-stop shopping” imaging approach where the whole vasculature from the heart over the aorta and into the carotids and their branches is done in addition to full tissue imaging: this method should make it possible to delineate ischemia and see occlusion.

As more and more data are being gathered, we are getting a more precise idea of what the “ideal” thrombolysis candidate looks like, and in what cases we might have to switch from one technique to the next or to even combine methods. This was shown recently in an elegant paper by Riedel *et al.*^[11] where they demonstrated that IV thrombolysis was less successful in patients where the thrombus length exceeded 8 mm. While this study was performed on unenhanced CTs and spontaneously hyperdense vessels were measured, it again shows on the one hand the power of unenhanced CT and on the other hand reveals that imaging can help to better triage patients towards an optimal therapy. Indeed, if we now know that beyond a certain length a thrombus may not respond to intravenous therapy, a more aggressive approach using interventional techniques with either intra-arterial pharmacological or mechanical thrombus therapy can be envisioned. Clinically, of course, the findings may still be refined by the use of angio-CT to measure length^[11].

After the intervention has been performed, it is important to obtain some kind of post-procedural imaging. The most standard method has been CT in order to exclude post-therapeutic hemorrhage. MRI will determine better the occurrence of post-ischemic and post-therapeutic events. With new developments in angiographic technology (among others, the advent of the so-called flat panel detector technology), it is possible to use the increase in resolution to reconstruct CT-like images; this provides the therapist (endovascular/surgical) with the possibility to directly perform CT on the angiography table and to monitor directly what is happening inside the brain.

Very often in the immediate post-procedural period, CT shows areas of diffuse increased density where it is difficult to differentiate contrast from blood. Double-energy CT should provide better delineation of contrast from blood in post-therapeutic CT: by analyzing the different images obtained with different peaks of radiation for the tubes, it is possible to differentiate between different tissue components.

In conclusion, while a lot has been done in imaging and in therapy for stroke treatment, optimal treatment is still reaching an inadequate percentage of the affected population. Strategies have to be developed so that the patients can reach the hospital in time and when there be taken care of by the stroke team in time. Only when these criteria are met will the whole stroke-related armamentarium be ready for the possibilities that are offered to our patients today. Unfortunately, we see from the paper cited above that only 41% of patients are imaged accordingly within 25 min of arrival^[2]. Since “time is brain”, and with a time window that is not excessively long, any minute lost before initiation of therapy is a neuronal disaster. Technologically, a lot has been done to decrease imaging time: a stroke CT or MR protocol can be performed with unenhanced images, perfusion and angiography in 15 to 20 min for both techniques. Recently, hopes have been raised greatly that eventually the use of different recanalization techniques might lengthen the therapeutic window: this has been the case for intra-cranial stent placement and/or thrombectomy. These techniques thus have the advantage that they may allow for treatment even in situations where we cannot compress lost time any further. Wherever the patient comes from, he has to be transported to the hospital and examined by a stroke specialist and, even if one tries to minimize this and imaging to a great extent, there is still a minimal time that can probably not be shortened. Another way to further reduce time is to somehow combine imaging and intervention by either initiating thrombolysis in the scanner or by transforming the angiography unit into a scanner, as some studies have demonstrated to be possible^[6,7]. The overall aim is to more quickly identify the patients and to have them reach imaging and a stroke unit as fast as possible.

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