COMPARATIVE OVERVIEW OF BRAIN PERFUSION IMAGING TECHNIQUES

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Summary
Numerous imaging techniques have been developed and applied to evaluate brain hemodynamics. Among these are: Positron Emission Tomography (PET), Single Photon Emission Computed Tomography (SPECT), Xenon-enhanced Computed Tomography (XeCT), Dynamic Perfusion-computed Tomography (PCT), Magnetic Resonance Imaging Dynamic Susceptibility Contrast (DSC), Arterial Spin-Labeling (ASL), and Doppler Ultrasound. These techniques give similar information about brain hemodynamics in the form of parameters such as cerebral blood flow (CBF) or volume (CBV). All of them are used to characterize the same types of pathological conditions. However, each technique has its own advantages and drawbacks.

This article addresses the main imaging techniques dedicated to brain hemodynamics. It represents a comparative overview, established by consensus among specialists of the various techniques. For clinicians, this paper should offer a clearer picture of the pros and cons of currently available brain perfusion imaging techniques, and assist them in choosing the proper method in every specific clinical setting.

Key words: brain perfusion, stroke, brain tumor, imaging techniques, comparative study.

Résumé
Revue comparative des techniques d’imagerie de la perfusion cérébrale
De nombreuses techniques ont été développées et appliquées à l’étude de l’hémodynamique cérébrale. Parmi ces techniques, citons: la Tomographie par Émission de Positrons (TEP), la Tomographie par Émission par Photon Simple (TEPS), la tomodensitométrie à Xénon stable, le scanner de perfusion dynamique, l’imagerie dynamique de susceptibilité par résonance magnétique avec contraste, le marquage de spin artériel, et l’ultrason Doppler. Ces techniques donnent des informations similaires concernant l’hémodynamique cérébrale sous la forme de paramètres tels que le débit sanguin cérébral ou le volume sanguin cérébral. Toutes ces techniques sont utilisées pour caractériser les mêmes types de désordres de la perfusion cérébrale. Toutefois, chaque technique a ses propres avantages et inconvénients.

Cet article présente les principales techniques dédiées à l’étude de l’hémodynamique cérébrale. Il représente une revue comparative, réalisée en consensus par des spécialistes des différentes techniques. Cet article devrait permettre aux utilisateurs cliniciens d’avoir une vision plus claire des avantages et des inconvénients des différentes techniques d’imagerie de la perfusion cérébrale disponibles à l’heure actuelle. Il devrait les assister dans le choix de la méthode adéquate pour une situation clinique donnée.

Mots-clés : perfusion cérébrale, accident vasculaire cérébral, tumeur du cerveau, techniques d’imagerie, études comparatives.

Numerous imaging techniques have been developed and applied to evaluate brain hemodynamics. The main imaging techniques dedicated to brain hemodynamics are: Positron Emission Tomography (PET), Single Photon Emission Computed Tomography (SPECT), Xenon-enhanced Computed Tomography (XeCT), Dynamic Perfusion-computed Tomography (PCT), Magnetic Resonance Imaging Dynamic Susceptibility Contrast (DSC), Arterial Spin-Labeling (ASL), and Doppler Ultrasound. Most of these techniques rely on mathematical models developed at the beginning of the century [1-4]. All these techniques give similar information about

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A quantitative CBF map can be calculated from a mathematical model applied to this dataset. A technical description, including what kind of contrast is used and whether radiation is required, will be followed by a discussion of the technical requirements. Notably, the duration of a routine study will be addressed. Then will come an in-depth discussion of the interpretation of the results, including a description of the underlying mathematical model, the duration of the data post-processing, the measured parameters, the accuracy of the values in normal parenchymal pixels, in pixels containing large vessels and in pathological pixels with altered hemodynamics, and the reproducibility of the technique. The feasibility of the technique in children and at bedside will also be addressed, as well as the afforded brain coverage and spatial resolution, and the minimal time interval between two successive studies. Finally, the typical clinical applications will be reported, as well as the availability of the technique in the emergency setting.

**Technical description**

Positron Emission Tomography (PET) is a non-invasive diagnostic tool that provides tomographic images of quantitative parameters describing various aspects of brain hemodynamics, including rCBF, rCBV, regional oxygen extraction fraction (rOEF), cell viability, but also proliferation and/or metabolic activity of tissues, regional cerebral metabolic rate of oxygen (rCMRO₂), or glucose (rCMRGl), neurotransmission processes, etc. These images result from the use of different substances of biological interest labeled with positron emitting radioisotopes (PET radiopharmaceuticals).

The PET tracers used for the measurement of CBF are: $_{15}$O₂, $^{15}$C$_{O}$, and $^{15}$H$^{2}_O$. $^{15}$H$^{2}_O$ is administered directly by intravenous injection; a 1-2 minute scan is performed, and its results combined with an arterial blood sampling measurement serving as an input function; application of the Kety-Schmidt model to this dataset leads to quantitative CBF maps [5, 6]. $^{15}$C$^{15}$O is inhaled continuously during 8-10 minutes; the catalytic action of carbonic anhydrase in the pulmonary vasculature resulting in rapid transfer of the $^{15}$O label to $^{15}$H$^{2}_O$; a 1-2 min scan is performed once a steady-state is reached; the same approach as the one described above is used to calculate a quantitative CBF map [7].

Successive inhalation of $^{15}$O, $^{15}$C$_{O}$, and $^{15}$H$^{2}_O$ over 60 minutes allows to measure the rCBV, the rCMRO₂, as well as the rOEF, which designates the fraction of the oxygen delivered to brain (approximately 40% [3] is extracted by the brain parenchyma and metabolized [8-10]. $^{18}$F-fluorodeoxyglucose (FDG) PET can measure the regional glucose consumption of the living tissues, and now widely used for the evaluation of cancer with whole body scanning. Additionally, it is a reliable method to detect a regional metabolic deficit in the brain [11, 12].

PET radiopharmaceuticals are cyclotron products and have a very short half-life ($^{18}$F: 1.7 hrs, $^{15}$O: 2 min, $^{11}$N: 10 min, $^{11}$C: 20 min). Whole-body radiation exposure by PET examination is usually 0.5 – 2.0 mSv per scan. The radiation dose may differ among institutions depending on the protocol or quality of PET camera. The duration of the data acquisition depends on the selected method and tracer. It typically ranges around 5-9 minutes for a routine clinical study.

**Technical requirements**

In addition to the access to cyclotron PET radiopharmaceuticals, PET imaging requires a PET camera or scanner, usually consisting of several full rings detectors BGO (Bismuth Germanate Orthosilicate), LSO (Lutetium Orthosilicate) or GSO (Gadolinium Orthosilicate). Variations on this basic design include partial ring BGO dedicated PET scanner and dedicated PET scanner with six position-sensitive sodium iodide detectors. A hybrid PET-CT gives the opportunity for accurate registration and exact correlation of PET functional aspects with anatomical findings. These cameras are much faster (~ 4 times) than the older generation of PET cameras.

**Interpretation**

As described above, PET measurements of CBF are mainly performed using 1) the bolus injection of $^{15}$H$^{2}_O$ of or by 2) the continuous inhalation of $^{15}$C$^{15}$O. In both methods, CBF can be quantified based on Kety-Schmidt equation [10]. PET results consist in maps describing CBF, CBV (CBV is calculated from the ratio of the radioactivity in brain to that in peripheral whole blood), rOEF, and rCMRO₂ values. Data processing to obtain these maps typically takes 5-10 minutes. PET results can be visually interpreted on a computer screen. Correlation with structural information (CT, MRI) is highly desirable for accurate interpretation [13]. Quantification advantageously completes the visual interpretation and allows to objectively assess changes in post-intervention or follow-up studies. The main advantage of PET technique lies in this quantitative accuracy, even in pixels containing large vessels and in brain regions with altered brain perfusion or metabolism. PET results
## Table I. – Overview of the imaging techniques dedicated to brain hemodynamics.

<table>
<thead>
<tr>
<th>Brain Perfusion Imaging Techniques</th>
<th>PET</th>
<th>SPECT</th>
<th>XeCT</th>
<th>PCT</th>
<th>DSC</th>
<th>ASL</th>
<th>Doppler</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Feasibility</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Age range</strong></td>
<td>adults</td>
<td>adults</td>
<td>adults</td>
<td>adults</td>
<td>adults</td>
<td>adults + children</td>
<td>adults + children</td>
</tr>
<tr>
<td>Cerebral (and children for static exams)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bedside</strong></td>
<td>no</td>
<td>in some instances</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td><strong>Contrast material</strong></td>
<td>15O2, C15O2, H215O</td>
<td>133Xe, 99mTc – HMPAO, 99mTc – ECD, 123I-IMP (diffusible)</td>
<td>stable xenon gas (diffusible)</td>
<td>iodinated contrast material (non-diffusible)</td>
<td>gadolinium chelate (non-diffusible)</td>
<td>none (endogenous contrast)</td>
<td>None (endogenous contrast)</td>
</tr>
<tr>
<td><strong>Radiation/study</strong></td>
<td>0.5-2mSv</td>
<td>3.5-12mSv</td>
<td>3.5-10mSv</td>
<td>2-3mSv</td>
<td>none</td>
<td>none</td>
<td>none</td>
</tr>
<tr>
<td><strong>Data acquisition</strong></td>
<td>5-9min</td>
<td>10-15min</td>
<td>10min</td>
<td>40sec</td>
<td>1 minute</td>
<td>5-10min</td>
<td>10-20min</td>
</tr>
<tr>
<td><strong>Data processing</strong></td>
<td>5-10min</td>
<td>5min</td>
<td>10min</td>
<td>5min</td>
<td>5min</td>
<td>5min</td>
<td>none</td>
</tr>
<tr>
<td><strong>Interpretation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mathematical model</strong></td>
<td>Kety-Schmidt model</td>
<td>Kety-Schmidt model</td>
<td>Kety-Schmidt model</td>
<td>Meier-Zierler model</td>
<td>Meier-Zierler model</td>
<td>Meier-Zierler model</td>
<td>other</td>
</tr>
<tr>
<td><strong>Assessed parameters</strong></td>
<td>CBV, CBF, rOEF, glucose metabolism</td>
<td>CBF</td>
<td>CBF</td>
<td>CBF, CBV, MTT, TTP, permeability map</td>
<td>CBF, CBV, MTT, TTP, permeability map</td>
<td>CBF</td>
<td>ICA BFV</td>
</tr>
<tr>
<td><strong>Large vessels</strong></td>
<td>no influence on results</td>
<td>no influence on results</td>
<td>no influence on results</td>
<td>influence results</td>
<td>influence results</td>
<td>no influence on results</td>
<td>not applicable</td>
</tr>
<tr>
<td><strong>Quantitative accuracy</strong></td>
<td>yes</td>
<td>yes for 133Xe and 123I-IMP</td>
<td>yes</td>
<td>yes</td>
<td>not in daily practice</td>
<td>yes</td>
<td>yes for hemispheric CBF</td>
</tr>
<tr>
<td><strong>Including low perfused areas</strong></td>
<td>yes</td>
<td>not applicable</td>
<td>yes</td>
<td>yes</td>
<td>not applicable</td>
<td>not below 10ml/min/100g</td>
<td>not applicable</td>
</tr>
<tr>
<td>Brain Perfusion Imaging Techniques</td>
<td>PET</td>
<td>SPECT</td>
<td>XeCT</td>
<td>PCT</td>
<td>DSC</td>
<td>ASL</td>
<td>Doppler</td>
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<td>---------</td>
</tr>
<tr>
<td>Reproducibility</td>
<td>5%</td>
<td>10%</td>
<td>12%</td>
<td>10-15%</td>
<td>10-15%</td>
<td>10%</td>
<td>5%</td>
</tr>
<tr>
<td>Brain Coverage</td>
<td>whole brain</td>
<td>whole brain</td>
<td>6-cm thickness</td>
<td>4-5cm thickness</td>
<td>whole brain</td>
<td>whole brain</td>
<td>one measurement for each hemisphere</td>
</tr>
<tr>
<td>Spatial resolution</td>
<td>4-6mm</td>
<td>4-6mm</td>
<td>4mm</td>
<td>1-2mm</td>
<td>2mm</td>
<td>2mm</td>
<td>not applicable</td>
</tr>
<tr>
<td>Minimal Time interval Between 2 Successive Exams</td>
<td>10min</td>
<td>10min</td>
<td>20min</td>
<td>10min</td>
<td>25min</td>
<td>0min</td>
<td>0min</td>
</tr>
</tbody>
</table>

(split-dose technique for $^{99mTc}$-HMPAO, $^{99mTc}$-ECD and $^{123I}$-IMP)

**Clinical Applications**

<table>
<thead>
<tr>
<th>Clinical fields</th>
<th>(acute and) chronic cerebrovascular disorders</th>
<th>acute and chronic cerebrovascular disorders</th>
<th>acute and chronic cerebrovascular disorders</th>
<th>acute and chronic cerebrovascular disorders</th>
<th>chronic cerebrovascular disorders</th>
<th>acute cerebrovascular disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>trauma</td>
<td>trauma</td>
<td>trauma</td>
<td>trauma</td>
<td>trauma</td>
<td>trauma</td>
</tr>
<tr>
<td>dementia and psychiatric diseases</td>
<td>vasospasm</td>
<td>vasospasm</td>
<td>vasospasm</td>
<td>neurodegenerative disorders</td>
<td>vasospasm</td>
<td></td>
</tr>
<tr>
<td>epilepsy</td>
<td>epilepsy</td>
<td>epilepsy</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>brain tumors</td>
<td>brain tumors</td>
<td>brain tumors</td>
<td>brain tumors</td>
<td>brain tumors</td>
<td></td>
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<tr>
<td>brain activation studies</td>
<td>brain activation studies</td>
<td>brain activation studies</td>
<td>brain activation studies</td>
<td>brain activation studies</td>
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</tr>
</tbody>
</table>

*Emergency setting* | no | In some instances | yes | yes | yes | yes | yes |

“**Influence of large vessels**” is meant to report for which imaging techniques the CBF values in pixels containing large vessels are significantly superior to the capillary CBF values that are of interest.

“**Quantitative accuracy in low perfusion areas**” is meant to report which imaging techniques are quantitatively accurate even in case of altered hemodynamics areas, for example in ischemic areas.
PET imaging is feasible in children, but is not available at bedside. PET technique affords whole brain coverage. The spatial resolution of PET studies ranges around 4-6mm. The minimal time interval between two successive examinations ranges around 10 minutes for $^{15}$O labeled compound.

**Clinical applications**

Because not possible in the emergency settings, PET is used mainly in chronic clinical conditions. Chronic cerebrovascular disorders (figure 1) are the most frequent application of CBF and rOEF measurements. In patients with chronic internal carotid artery occlusion, elevated rOEF values are now considered as a major key indicator for predicting future impending infarction and determining the indication for bypass surgery [16-18]. Other PET applications are on brain tumors and epilepsy (figure 2), as well as, to a lesser extent, dementia, movement disorders, and brain activation studies (functional mapping studies). PET may be used for research purposes to validate other brain perfusion methods [19].

**SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY (SPECT) – KATALIN BORBÉLY, TADASHI NARIAI**

**Technical description**

Single Photon Emission Computed Tomography (SPECT) is a non-invasive technique generating tomographic images of the three-dimensional distribution of a specific radiopharmaceutical, which, depending on its nature, may reflect regional cerebral hemodynamics, dopamine or other transporter distribution, etc. [21].

$^{133}$Xenon ($^{133}$Xe) is historically the most important method for measuring brain hemodynamics [22]. However, the gamma rays emitted by $^{133}$Xe are of low energy, resulting in abundant scatter and limited spatial resolution. Consequently, retention tracers, such as $^{99m}$Tc-HMPAO, $^{99m}$Tc-Bicisate (Ethyl cysteine dimer ECD) and $^{123}$I-IMP, are more commonly used in clinical SPECT imaging of brain hemodynamics. The doses used in adults are typically 20 miliCuries (mCi) for HMPAO, 30mCi for ECD and 5mCi for $^{123}$I-IMP. These activities represent effective dose of 6.88, 12.21 and 3.53mSv, respectively.

Using retention tracers, the total scan time for a SPECT examination is about 10-15 minutes, depending on the imaging device. The goal is to achieve a total of counts superior to 5 million. Compared to step and shoot technique, the continuous acquisition mode may shorten the total scan time and reduce the mechanical wear of the system. Segmentation of the data acquisition into multiple sequential acquisitions allows exclusion of bad data, e.g. removing segments of projection data with motion artifacts.

**Technical requirements**

Multiple-detector (three- or four-headed) or other dedicated SPECT cameras for brain imaging should be used for the data acquisition, because they afford superior results compared to single- or two-headed cameras. Use of high-resolution collimation is recommended. The detector pan- and zoom-capabilities are often used to ensure that the...
entire brain is included in the field of view while allowing the detector to clear the patient’s shoulders [23].

Reconstruction of two-dimensional images from the projection data collected by the SPECT cameras is usually performed by filtered back projection (FBP). In addition to FBP, different algorithms have been developed to correct for photon attenuation, a possible source of image distortion. The most recent correction techniques are based on measured attenuation maps utilizing transmission scans to reveal an attenuation map specific to each patient. Scattering of the photons in the body of a patient is another important source of error in quantification of activity distribution. The amount of scatter can vary between 10% and 60% of the detected events. Different techniques, such as pulse height analysis (PHA), use of multiple energy windows, or deconvolution, allow to subtract the scatter from the projection data before the image reconstruction. Finally, several iterative reconstruction methods such as ordered subsets expectation maximization (OS-EM) have been recently proposed to correct images for artifacts and noise. Starting from an “initial guessed counts distribution” in the voxel grid or from an already created FBP image, the OS-EM algorithm elaborates iteratively the image grid, the final endpoint being to reach a state in which each pixel contains the number of counts it was containing in the raw matrix [23, 24].

**Interpretation**

Data processing relies on the microsphere principle for the Tc-99m tracers, and on the Kety-Schmidt model for the 133Xe and 123I-IMP, leading to the calculation of rCBF maps. Data processing typically takes 5 minutes.

The rCBF maps obtained with SPECT can be statistically evaluated in comparison to the normal control to depict the regions with abnormal perfusion. If SPECT results are fairly reproducible (10%), they are not quantitative in the current standardized settings. Particularly, the uptake of 99mTc-HMPAO is not linearly related to CBF, requiring special correction [25]. An exception is 133Xe SPECT technique, which uses a single detector positioned over the right lung to measure an arterial input function and to calculate quantitative CBF values.

**Feasibility**

SPECT technique can be used at bedside, and is feasible in children. One specific bedside indication for SPECT is seizure. As SPECT uses a retention tracer for measurement of cerebral perfusion, the radiopharmaceutical can be administered at the moment of the seizure, and imaging performed later, after stabilization of the patient, in order to identify the active epileptic focus.

SPECT affords whole brain coverage. The typical spatial resolution of SPECT studies is 4-6 mm. In case of challenges (acetazolamide), 133Xe SPECT examinations can be repeated, and the split-dose technique can be used for 99mTc-HMPAO, 99mTc-ECD and 123I-IMP, with administration of two half doses, one hour apart from each other. The obtained images are subtracted from each other.

**Clinical applications**

The main indications for SPECT studies are: acute and chronic cerebrovascular diseases, and presurgical localization of epileptic foci.

Perfusion SPECT provides valuable information in acute stroke with respect to complications [26], outcome [27, 28] or choice of treatment strategy [29]. In chronic cerebrovascular disease, SPECT assessment of functional reserve capacity may guide decisions regarding vascular surgery [30, 31].

Ictal SPECT studies (eventually complemented by interictal investigations) are indicated in focal epilepsy for the localization of the epileptic focus prior to epileptic surgery [32].

SPECT has also been reported to show abnormalities in head trauma patients [33, 34] and in a variety of psychiatric disorders (such as major depression, post-traumatic stress disorder and schizophrenia),

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**Fig. 2.** – 42-year-old female with frontal lobe epilepsy. Subtraction of interictal from ictal 99mTc-Ethyl cysteine dimer (ECD) SPECT images, and co-registration with the patient’s MRI identify the epileptic focus more conspicuously than 18fluorodeoxyglucose (FDG) PET images.

**Fig. 2.** – Patiente de 42 ans avec une épilepsie du lobe frontal. Les images ictale et interictale obtenue par Tomographie d’Emission par Photon Simple à 99mTc-Ethyl cysteine dimer (ECD), une fois soustraites et recalées avec les images par résonance magnétique, permettent d’identifier le foyer épileptogène plus précisément que les images Tomographie par Emission de Positrons à 18fluorodeoxyglucose (FDG) PET images.
and to afford early detection and differential diagnosis of dementia [35, 36]. Perfusion SPECT may provide helpful information in viral encephalitis (e.g. herpes simplex encephalitis), vasculitis and HIV-encephalopathy [37, 38]. Finally, SPECT assessment of arrest of cerebral perfusion is an accurate technique to confirm brain death [39].

**XENON-ENHANCED CT (XeCT)**

– **MUSA SESAY, HOWARD YONAS**

**Technical description**

Xenon-enhanced CT (XeCT) has been used for over 20 years to evaluate quantitative cerebral blood flow (CBF) in humans [40]. Stable (non-radioactive) Xenon is inhaled and serves as contrast material. The Xenon gas rapidly dissolves in blood, freely crosses the lipid-rich blood brain barrier, and enters the brain. CBF is calculated by using the modified Kety-Schmidt equation that integrates the following parameters: the time course of the concentration of Xenon in the blood and brain, and the blood-brain partition coefficient (or lambda) for Xenon [41]. The concentration of Xenon in the brain is measured directly by the CT scanner. The concentration of Xenon in arterial blood is determined indirectly and accurately from the end-tidal Xenon provided that the pulmonary function is not severely impaired [42]. The current technique requires the inhalation of a mixture of Xenon (28%) and oxygen (21-60% as clinically indicated) within a data acquisition period of 4.3 minutes [43]. Following the acquisition of a baseline scan of the entire head, four to six contiguous 10 mm-thick levels are selected for CBF measurement. Each level is scanned 6 times during the inhalation period, with exact table relocation. At the end of inhalation Xenon is rapidly washed out from cerebral tissues (half-life about 40 seconds).

Adverse reactions to stable Xenon like nausea, reversible alteration of sensorium or respiratory depression have been reported in <0.1% of cases [44]. In addition, patient motion is a serious limitation to the technique. It can produce artifacts, making interpretation difficult and inaccurate. Head immobilization devices, sedation in some patients, and lowering the Xenon concentration to 28% has lessened the incidence of motion artifacts [43]. Patients with severe respiratory disease, patients with full stomach, ventilated patients with a tidal volume less than 250ml, and restless patients who cannot be adequately sedated should be excluded from XeCT studies.

The average radiation dose to the brain from a typical study in an adult ranges from 3.5 to 10mSv [45].

**Technical requirements**

XeCT technology requires a CT scanner and a Xenon delivery system (ENHANCER™, DDP USA or XETRON™, ANZAI, Japan). The latter is a compact and fully mobile unit that can be moved between CT suites. It houses the disposable Xenon gas cylinders. A wall outlet source or an oxygen tank can be used for oxygen delivery. The machine is equipped with continuous monitors of CO₂, O₂ and Xenon integrated within a low resistance respiratory circuit that is initially open to room air, then partially open and finally closed upon utilizing. The later feature is vital for limiting the use of Xenon to less than 5 liters per study. The monitors not only provide a means of maintaining inhaled Xenon and O₂ within 1% of prescribed concentration, but also function as a monitor of apnea. Studies are easily accomplished with a mask or via connection to an endotracheal tube with the patient's volume ventilator being used to maintain ventilation through the enhancer [43].

The medical grade Xenon is available and distributed worldwide. In the U.S., however, Xenon is not currently approved by the FDA. The technology is only available at this time under IND status (Investigational New Drug).

**Interpretation**

As mentioned above, XeCT technique relies on the Kety-Schmidt equation to extract from the acquired data quantitative information about CBF and the partition coefficient, lambda, between blood and tissue [46]. Superimposition of the numerical data on the anatomic image yields a high-resolution (Full Width Half Maximum [FWHM] <4mm) map of quantitative flow data that is tightly coupled to cerebral anatomy [47]. With the addition of a gray or color scale, the data is converted to a map for visual inspection, on which regions of interest (ROIs) can be drawn for regional CBF quantitative assessment within a wide spectrum of CBF values (0-140ml/100g/min). A confidence map is also produced to demonstrate the effects of any patient motion and other artifacts on the data. The data processing requires approximately 10 minutes.

Although the stability of the flow value in a single voxel of 10mm³ is poor, the reliability of the data from an ROI of >100 voxels is approximately 12%. This reliability despite the pharmacological property of Xenon to directly increase CBF by 20-30% is explained by the fact that nearly all the important flow data is acquired prior to this flow activation (the latter becomes significant only after 2.5 minutes of inhalation) [48]. Reliability is also increased by the use of a flow phantom that permits standardization of the data and the calibration of scanners from different manufacturers.

**Feasibility**

Because of this radiation risk, XeCT in children is only recommended after careful consideration of the potential risks and benefits. XeCT does not afford whole brain coverage, but still four to six contiguous 10mm-thick slices can be evaluated. The minimal time interval between two successive examinations ranges around 10 minutes. XeCT challenge studies, for example for measuring the vasodilatory response to acetazolamide, can thus be performed in an outpatient setting within 30 minutes [43] (figure 3).
Clinical applications

Cerebrovascular disorders are the main clinical application of XeCT, which has the ability to provide measurements of equal validity within the cortex as well as the depth of the brain that can determine proximity to the ischemic threshold [49]. Large clinical series of balloon test occlusion have demonstrated the ability of XeCT to select the patients who require bypass surgery prior to vascular sacrifice [50]. XeCT has also been shown useful in understanding the heterogeneity of flow alterations following closed head injury, providing important insights into the efficacy of therapies designed to improve CBF [51].

As mentioned above, the short half-life of inhaled Xenon makes XeCT CBF particularly adequate for repeat (challenge) tests to study cerebrovascular physiology (figure 3). Cerebrovascular reserve (CVR) assessed by examining the quantitative response of flow in patients with occlusive vascular disease has provided a means for identifying high-risk subgroups [52]. The efficacy of blood pressure elevation has been monitored in patients with post subarachnoid hemorrhage vasospasm [53]. For patients with elevated intracranial pressure following closed head injury, the ability to monitor the local, regional and global effects of pCO2 lowering has provided specific data as to the safety and efficacy of CO2 manipulation [54].

DYNAMIC PERFUSION-CT (PCT)
– JAMES D. EASTWOOD, WILLIAM P. DILLON, MAX WINTERMARK

Technical description

Dynamic perfusion-CT (PCT) is a technique for measuring brain hemodynamics that uses first-pass tracer methodology following bolus infusion of intravenous iodinated contrast material. Typically, continuous cine scanning is performed during a total scanning time of 40-45 seconds, with a scan rate of 1 image per second. The bolus, typically 40-50cc of 300-370mg/dl iodinated contrast material is administered via an arm vein [55].

Although one would expect a higher radiation dose with PCT than standard unenhanced CT, it is necessary to recall that low mAs (100-150mAs) and/or kV protocols (80-90kVp) are typically used for PCT studies to limit dose. The effective radiation dose involved in a PCT series ranges around 1.6-2.0mSv (versus 2.5mSv for a standard unenhanced CT of the brain) [56]. Iodinated contrast is safe as long as not utilized in patients with renal failure or diabetes mellitus [57].

Technical requirements

For adequate PCT data acquisition, a helical CT scanner capable of operating in the cine mode is needed. Multislice CT scanners offer the advantage of greater tissue coverage per acquisition (usually 2cm) compared with single slice CT scanners (typically 1cm). In case of a protocol using two successive bolus administrations, a total coverage of 4-5cm can be achieved [55].

An automatic injector of contrast material capable of at least 3-4cc/second infusion rates is also necessary for an adequate PCT examination, in order to obtain a short bolus. Such injection rate requires a peripheral venous access with a catheter size of at least 22 gauge (20 or 18 gauge may be optimal) [58].

Interpretation

PCT data processing that can typically be achieved in 5 minutes is performed with a post-processing software using either rate-of-upslope estimation of CBF (for infusion rates above about 6cc/sec) or deconvolution analysis (for infusion rates of 4-5cc/second). Only deconvolution analysis leads to quantitatively accurate results, including in areas with low perfusion [59]. PCT technique however...
overestimates brain hemodynamics values in pixels including large vessels [60].

Ideally, images of CBF, CBV, and mean transit time (MTT) are interpreted together on a workstation permitting the use of visual assessment combined with quantitative analysis with ROIs. Regions of decreased hemodynamics are often represented as regions of prolonged MTT. MTT maps have the property of generally being quite sensitive to the presence of altered brain hemodynamics. Comparing CBF, CBV, and MTT values between abnormal regions and mirror-image control regions is an effective method of measuring the degree of underperfusion present in a given case or location. Generally, CBF values can be interpreted using thresholds established using other methods, notably XeCT [61, 62]. Another way to proceed is to apply the concept autoregulation and to evaluate simultaneously MTT and CBV maps. Within areas with prolonged MTT, the regions with increased CBV resulting from vasodilatation and collateral recruitment are considered to have preserved autoregulation and to represent “tissue at risk”, whereas regions with decreased CBV correspond to the infarct core [63, 64] (figure 4).

**Feasibility**

It is presently not possible to perform a PCT examination at the bedside. The patient must be transported to the CT department [55].

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**FIG. 4.** – 55-year-old male patient admitted for right homonymous hemianopsia and right-body sensory loss. The admission noncontrast CT, obtained 6 hours after symptom onset, was considered as unremarkable, except for a dense left posterior cerebral artery (PCA) (arrowheads). Perfusion-CT (PCT) demonstrates prolonged mean transit time (MTT) and reduced regional cerebral blood flow (rCBF) values in the left PCA territory. Regional cerebral blood volume (rCBV) values, however, are reduced only in a small part of the left thalamus, but increased in the rest of the PCA territory. These areas correspond to infarct and penumbra, shown in red and green, respectively. The admission CT-angiogram demonstrates an occluded left P1 segment that is recanalized, but remains focally stenotic, on the follow-up MR-angiography obtained 3 days later. The follow-up diffusion-weighted imaging examination demonstrates a completed stroke in the predicted infarct core in the left thalamus. The penumbra as depicted on the admission PCT did not infarct, most likely as a result of early recanalization.

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**FIG. 4.** – Patient de 55 ans hospitalisé en raison d’une hémianopsie homonyme droite et d’un hémisyndrome droit. Le scanner sans contraste obtenu à l’admission, 6 heures après le début des symptômes, fut considéré comme normal, à l’exception d’une artère cérébrale postérieure gauche dense (têtes de flèche). Le scanner de perfusion démontre un temps de transit moyen prolongé et un débit sanguin cérébral régional diminué dans le territoire de l’artère cérébrale postérieure gauche. Toutefois, le volume sanguin cérébral régional est diminué seulement dans une petite portion du thalamus gauche, et augmenté dans le reste du territoire de l’artère cérébrale postérieure gauche. Ces deux régions correspondent à l’infarctus et à la pénombre, respectivement. L’angiographie par scanner met en évidence une occlusion du segment P1 gauche, qui est recanalisé mais avec une sténose focale résiduelle, sur l’angiographie par résonance magnétique de suivi obtenue 3 jours plus tard. L’examen de diffusion de suivi révèle un infarctus complet dans la région prédite comme telle dans le thalamus gauche. La pénombre telle que démontrée sur le scanner de perfusion à l’admission n’a pas évolué vers l’infarctus, le plus probablement en raison d’une recanalisation précoce.
PCT has a limited spatial coverage (20 to 48-mm thickness). However, the issue of spatial coverage will be addressed in the near future through the development of multislice CT scanners with greater arrays of elements. Even presently, PCT has demonstrated 95% accurate in the delineation of the extent of supratentorial strokes despite its limited spatial coverage [65].

The minimal time interval between two successive perfusion-CT series is 3-6 minutes, allowing to perform two successive perfusion-CT series in the same study in order to increase spatial coverage, and to combine PCT imaging with vasodilatory challenge (e.g., acetazolamide challenge) [66].

Clinical applications

PCT can rapidly detect the size of hypoperfused regions in the setting of acute stroke [61-64]. At the time of this writing, definitions of infarct core and penumbra are undergoing active research to provide understanding of how the method could potentially be used to guide therapy. Anecdotally, in the setting of unilateral carotid occlusion, PCT imaging may be combined with vasodilatory challenge (e.g., acetazolamide challenge) to permit identification of tissue at risk for future infarction. Baseline imaging may reveal increased MTT, increased CBV (due to vasodilatation) and decreased CBF. Following acetazolamide infusion, further decrease in CBF is observed in tissue at risk for ischemia without intervention [66].

PCT may be helpful for observing the effects of focal vasospasm following subarachnoid hemorrhage [67, 68].

Finally, PCT can also be used in head trauma patients as a prognostic factor [69], as well as to guide management of intracranial pressure in these patients [70].

The wide availability of CT scanners in the emergency departments (ED) and the short duration of PCT examinations make PCT an ideal technique for ED patients, including both stroke patients and head trauma patients [69-71].

DYNAMIC SUSCEPTIBILITY-WEIGHTED (DSC) BOLUS-TRACKING MAGNETIC RESONANCE IMAGING – CÉCILE B. GRANDIN, SALVADOR PEDRAZA

Technical description

Dynamic susceptibility contrast imaging (DSC) relies on the measurement of the T2 or T2* decrease during the first pass of an exogenous endovascular tracer through the capillary bed [72, 73]. The technique requires ultrafast imaging such as echo planar imaging (EPI), principles of echo-shifting with a train of observations (PRESTO) or spiral imaging. Gradient echo (GRE) or spin echo (SE) sequences can be used, but the signal change measured with GRE (∆T2*) is greater than that measured with SE (∆T2), allowing one to use a shorter echo time (TE) and a lesser amount of contrast agent. The sequence duration is about 1 minute and the sampling rate (repetition time (TR) of the sequence) should be kept below 2 sec. This can be achieved with GRE sequences for whole brain coverage (up to 24 slices) [74]. The used tracer is a conventional chelate of gadolinium, injected through an 18G catheter into a peripheral vein at a regular dose of 0.1mmol/kg for GRE or 0.2mmol/kg for SE, and at an injection rate of 5 to 10ml/sec, immediately followed by a 20-30ml saline flush [72].

DSC does not expose patients to ionizing radiation. Intolerance to gadolinium chelates is very rare. The contraindications are those of MRI in general: pacemakers and some other implanted metallic or electronic devices, obesity (more than 150kg). Fixed ferromagnetic dental devices and intracranial clips generate prominent artifacts. Claustrophobia or agitation may require sedation.

Technical requirements

Most 1.5 T MR scanners are now equipped with the fast-imaging capabilities required for DSC. The use of a power injector is recommended.

Interpretation

DSC relies on the application of the indicator dilution theory [4]. In case of blood-brain barrier rupture, the indicator dilution theory must be modified and a measure of the permeability must be introduced [75]. For qualitative hemodynamic measurements, a pre-load dose of contrast before the bolus is an easier way to minimize the effect of contrast leakage.

Using commercially available softwares, various parameters can be calculated in a few minutes from the time-intensity curves measured in each pixel, allowing one to reconstruct parametric maps. The most commonly calculated parameters are: time-to-peak (TTP), apparent MTT (apMTT), corresponding to the first moment of the curves, CBV calculated from the area under the curve, and CBF index (CBFi), equal to CBV/apMTT. These maps do not afford quantitative assessment of brain hemodynamics, but provide indicators of hemodynamic disturbances that are very useful in a clinical setting. They can be interpreted visually or semi-quantitatively by calculating the ratio or difference between the values in a ROI placed in the abnormal area and a mirror ROI placed in the contralateral area considered as a normal reference. Note that, for the moment, there is no standardization in the interpretation of the DSC parametric maps [77].

The quantification of CBF by DSC requires the deconvolution of the measured tissue curves by an arterial input function (AIF) [78, 79]. If the AIF is adequately calibrated, absolute quantitative CBV and CBF maps can be obtained [80]. This step is more complex with DSC than with PCT because the relationship between the signal intensity and the gadolinium concentration is not always linear [81]. Several studies have demonstrated a good correlation between the absolute CBV and CBF values obtained according to this approach as compared to PET or XeCT [82-84]. Note that, in order to inter-
pret the DSC perfusion maps quantitatively or semi-quantitatively, it is necessary to mask out the large vessels (very prominent with GRE sequences). Low perfusion values can be accurately measured until 5mL/min/100g. Under this level, the signal-to-noise ratio becomes too low for a precise quantification [85]. The reproducibility of the method ranges around 10-15% [86].

Feasibility

DSC has no age limitation and can be performed in children. MRI is not a bedside technique. It is not available at night and during weekends in many institutions.

A spatial resolution around 1.5x1.5x4mm is routinely available, but the actual in-plane resolution is usually closer to 2mm considering the degradation of the point spread function during the bolus passage [73].

A delay of 25min between successive contrast injections has been shown to be sufficient for repeated CBF measurements, allowing one to assess the cerebral vascular reserve. This delay may be longer for successive CBV measurements [86, 87].

Clinical applications

The main clinical applications of DSC are acute stroke, chronic cerebrovascular disease, and tumors.

MRI can be performed in the emergency setting of hyperacute stroke. DSC is used in association with diffusion-weighted imaging (DWI) and magnetic resonance angiography (MRA) for the early evaluation of stroke patients. Prolonged TTP and MTT values are the most sensitive features to detect a hemodynamic disturbance. CBV and CBF maps are more difficult to visually interpret (especially in white matter) but better reflect of brain perfusion [88-90]. A threshold can be applied to DSC maps in order to identify the area at risk for infarction and predict outcome, but no consensus has been achieved regarding the specific thresholds that might distinguish reversible and irreversible ischemia [91, 92]. The presence of a mismatch (DSC abnormality larger than the diffusion abnormality), vessel occlusion on MRA and absence of hemorrhage should prompt thrombolytic treatment [93-95] (figure 5). DSC has also been successfully used to assess the cerebrovascular reserve [85, 96] and vasospasm [97].

In the management of patients with brain tumors, DSC can be combined with fine anatomic imaging, DWI, spectroscopy... providing the most comprehensive information in one examination and leading to a high ratio benefit-cost [98, 99]. DSC can differentiate high-grade glial tumors with neovascular proliferation and high CBV values, with respect to low-grade glial tumors with low CBV. DSC can also evaluate the response to treatment (CBV decrease), differentiate tumor recurrence (high CBV) from radiation necrosis (low CBV), and distinguish tumor (high CBV) from infection (low CBV, but depending on the etiology) or tumefactive multiple sclerosis lesions (low CBV) [100-102].

ARTERIAL SPIN LABELING (ASL)
– EMMANUEL BARBIER, GREG ZAHARCHUK

Technical description

Arterial spin labeling (ASL), also called arterial spin tagging, relies on the detection of magnetically labeled water. Once the magnetization of the inflowing water has been modified (generally inverted) upstream, it induces a small MR signal change downstream (a few percent of the tissue magnetization). Meanwhile, the magnetization of the perfusion tracer – i.e. the labeled water – is rapidly relaxing: the return of the longitudinal magnetization towards its equilibrium values takes a few seconds in the best cases (time constant T1) [103, 104].

Numerous ways to do the spin labeling have been described [105-107]. The existing techniques can be sorted out in two categories: pulsed techniques and continuous techniques, depending on how the spin labeling is performed. In both cases, a certain amount of blood magnetization is labeled before it irrigates the tissue of interest. With a "pulsed labeling" technique, the labeling is obtained by inverting the blood water magnetization in a thick slab of tissue located next to the slices of interest using a short (a few milliseconds) shaped RF pulse. To better define the tail of this inverted blood bolus, a saturation pulse can advantageously be used [108]. With a "continuous labeling" technique (figure 6), the labeling is performed continuously (during a few seconds) at the level of a plane through which blood flows (for the brain, this plane is located at the carotid level) either with the same coil or with a separate RF coil [109]. Finally, a recent approach has been proposed where the blood magnetization is selectively inverted based on the blood velocity. This new pulsed technique differs from the classical pulse inversion and opens a new range of possibilities [110, 111].

The different ASL techniques share one characteristic: no contrast media is needed. ASL uses endogenous water as a tracer. A typical acquisition lasts between 5 and 10 minutes depending on the scanner quality (magnetic field, RF coil sensitivity, etc.). Multiple pairs of label and control images are averaged together in order to obtain the required signal-to-noise ratio.

Technical requirements

Performed in MRI scanners, arterial spin labeling requires that the subject can be placed in a magnetic field and hence patients are subject to MRI contraindications. Since ASL is a subtraction technique, it is very sensitive to subject movement. Recently, background suppression techniques have been proposed, where the static tissue signal is reduced as far as possible. In these approaches, the sensitivity of the technique to motion is greatly reduced [112, 113].

Interpretation

For both pulsed and continuous types of technique, a control acquisition is necessary. The control acquisition has to yield the same tissue signal but
without inverting the blood magnetization. A simple subtraction between the averaged control and label images yields a flow-weighted map. Various models have been proposed to convert this flow-weighted image into a quantitative perfusion map. The data processing can be performed within a few minutes [103, 114-116].

The quantitative accuracy of the ASL technique has been addressed extensively in the literature. Computer simulations using an extensive model [117] and direct comparisons with other, non NMR, methods have been performed [115, 116, 118, 119]. It appears that blood flow is correctly estimated in the gray matter. In white matter, numerical simulations predict an overestimation while direct measurements show an underestimation. Quantitative ASL perfusion maps show a less than 10% change when rescanning the same subject [120].

The difference in signal between the label and control acquisitions is around 1% of the control images. Perfusion monitoring using ASL therefore requires a very high signal to noise ratio. As the signal difference is low, ASL cannot accurately map blood flow below ~10ml/100g/min. On the other hand, as flow increases (>150ml/100g/min), ASL will underestimate blood flow. This is due in part to the fact that the labeled blood leaves the voxel (reduced extraction fraction), as this can be observed in animal models [121].

In ASL techniques, the MRI sequences include spoiler gradients that suppress the signal arising from large vessels. Hence, ASL is not sensitive to large arteries or veins. The signal obtained with ASL comes mainly from water located in small vessels and in the surrounding tissue, due to the water exchange between blood and tissue [122].

In case of cerebrovascular disease, where the time for blood to travel from the labeling plane to the imaged plane is longer and may be spatially heterogeneous, special methods involving long
post-labeling delay times [123] or acquisition of images at multiple inversion times have to be implemented [121]. Even so, in the case of very long arrival times (e.g. when flow is provided by collateral networks), the magnetic label of the blood may be essentially completely relaxed, such that no information about perfusion can be reliably ascertained [124].

Feasibility

ASL examinations can be performed in any patient that can tolerate MRI. It is of particular interest for imaging cerebral blood flow in infants and children, given the lack of ionizing radiation or need for intravenous access.

Perfusion maps obtained with ASL can cover the entire brain. In humans, the typical voxel size is 2×2×4mm or 4×4×8mm. Since fast imaging techniques are generally used, it can be challenging to obtain a good image quality in regions with strong magnetic susceptibility gradients (i.e. magnetic field distortions), like the base of the brain near the frontal sinuses.

Successive ASL CBF maps can be acquired every other 5 to 8 seconds. ASL techniques can thus be successfully used for functional MRI applications, where control and label images are alternatively acquired [125-127].

Clinical applications

While ASL techniques have not entered widespread clinical usage, their utility has been demonstrated for a variety of acute and chronic cerebrovascular diseases. ASL is feasible for acute stroke patients and other emergency patients in hospitals with MRI access, assuming that they are stable enough to undergo an MRI examination.

Initial studies were performed in the setting of ischemic cerebrovascular disease (stroke and transient ischemia attack [TIA]), which demonstrated the feasibility of acquiring CBF maps using ASL in both the acute and chronic setting [128, 129]. Continuous ASL measurement of CBF reduction in the symptomatic hemisphere were shown to have high correlation with NIH stroke score [130]. ASL has also been used to study temporal lobe epilepsy [129] and brain tumor perfusion. A study of malignant gliomas demonstrated ASL perfusion imaging to be equally effective in determining tumor grade compared with DSC [131].

One significant advantage of ASL is the ability to perform multiple repeated measurements, as might be necessary before and after a cerebrovascular dilator (such as acetazolamide [132] (figure 7)), or before and after a neurointerventional procedure (such as carotid endarterectomy [133] or stenting). ASL methods also afford evaluation of functional
brain activation [134], useful for instance for the planning of neurosurgical procedures.

DOPPLER ULTRASOUND FOR BLOOD-FLOW-VOLUME MEASUREMENT IN THE INTERNAL CAROTID ARTERIES
– JEAN-FRANÇOIS SOUSTIEL,
THOMAS C. GLENN

Technical description

Numerous studies have shown the potential benefit of Doppler ultrasound related techniques for the investigation of cerebral hemodynamics. Although different in nature from other imaging techniques described hereby and accordingly limited for spatial resolution, Doppler ultrasound offers the advantage to be non-invasive and can be repeated as often as clinically indicated at the patient’s bedside. It does not involve radiation, does not require any contrast medium, and is free of any known adverse effect. In this regard, Ultrasound Doppler technology may represent a convenient tool for the measurement of blood flow volume (BFV) in the internal carotid artery (ICA) as a correlate for CBF in the corresponding hemisphere. Optimal BFV measurements of both ICAs are typically achieved within 10 to 20 minutes [135, 136].

Technical requirements

This technique, although implemented in most commercial Duplex machines since the early 1990s [135, 137] has not initially gained wide acceptance because of significant inaccuracy inherent to errors caused by the impact of angle-dependency on flow velocity and that of pulsatility on vessel diameter [138-140]. More recently, improvement in BFV measurements accuracy was achieved by combination of digital Doppler ultrasound and angle-independent dual-beam flow (ADBF) technology. This combination proved to be useful in order to overcome technical shortcomings of Doppler such as angle dependency and time-dependent variations in velocity profile and vascular diameter [141-144]. These requirements are obtained for instance with the Quantix-ND system (Cardiosonix-Neoprobe, Dublin, OH), which uses pulse-wave digital Doppler in order to integrate with a high resolution both temporal and spatial variations commonly overlooked by duplex imaging [142, 144].

Interpretation

ADBF is based on the simultaneous use of two ultrasound beams with a known geometrical configuration. Using dedicated digital Doppler technology, hundreds of sample volumes of less than 200µm length at successive depths are simultaneously sampled along each ultrasound beam. Full Fast Fourier Transform (FFT) analysis for each sample volume and application of an original algorithm allow real-time detection of flow velocity in the set of successive gates, followed by the determination of the chord segments that each beam traverses within the blood vessel. Since the angle between the two beams is known, the insonation angles of the two beams can be drawn from simple calculation based on trigonometric and Doppler considerations [144]. Further processing of the large number of small sample volumes allows determination of the pulsatile velocity profile and vascular diameter. Determination of the insonation angles allows calculation of absolute blood flow velocities, so that BFV can be directly obtained through integration of the velocity profile.
BFV levels can be calculated online and displayed on a monitor (figure 8), without any data post-processing needed. BFV measurements in the ICA may be used for the assessment of hemispheric or global CBF. Indeed, it shows a close and linear correlation with CBF in the corresponding hemisphere measured with $^{133}$Xe clearance technique [145, 146]. Admittedly, hemispheric CBF is not actually measured but estimated by BFV in the corresponding ICA based on the correlation between both parameters. Since this correlation is based on ICA BFV measurements, averaged CBF should not be confused with global blood flow, as BFV in the vertebro-basilar system is not taken into consideration.

Attention should be paid, as for any Doppler-based technique, to minimize user-related variations and errors. Accordingly, examination review should take into consideration the quality of the obtained signal and discard any recorded data compromised by artifacts. In particular, insonation angle should be kept between 55º and 65º induced. Further, discrepancies between the two channels measurements of diameter should be kept below 0.5mm for ICA diameter and 20% for ICA flow velocities. Under these conditions, reproducibility of the measurements has proved to be satisfactorily low with inter-observer variations ranging from 2.7 to 5.2%.

Clinical applications

BFV measurements in the ICA represent a convenient tool for a bedside evaluation of hemispheric and global CBF. The high flexibility of this technique allows the operator to fit without interference within the busy environment of an intensive care unit or emergency room, and obtain real time data on CBF dynamics of unstable patients.

BFV measurements in the ICA may represent a potentially useful tool for the investigation of vaso-motor response as part of the evaluation of cerebral occlusive disease and stroke, instead of less accurate transcranial Doppler [142]. BFV measurements of extracranial vessels may be of benefit in order to provide additional objective information about the cerebral hemodynamic effects of ICA occlusion [147-149]. BFV measurements are also useful to detected CBF impairment either due to increased intracranial pressure or vasospasm following traumatic brain injuries and subarachnoid hemorrhage, respectively [145]. In these critically ill patients, clinical changes may develop rapidly and be therefore overlooked by sparsely performed CBF imaging studies. Further evaluations of drugs influencing CBF such as anesthetics, mannitol and antihypertensive agents or any therapeutic measure may be of utmost importance for decision making, implying repeated CBF measurements within a short time. BFV measurements in the ICA fulfill adequately all these requirements.

CONCLUSION

Imaging techniques dedicated to brain perfusion all address the same types of pathological conditions, each having its own advantages and drawbacks (table II). PET is quantitatively accurate, but feasible only in very specific settings. Its main application at...
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<td>relatiively low signal-to-noise ratio per unit time</td>
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<td>high cost (however, cost-effective in well-established diagnostic algorithms)</td>
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<td>poor spatial resolution</td>
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<td>inhalation of Xenon via a face mask</td>
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<td>difficulties associated with obtaining MRI (claustrophobia, contraindications, and access issues)</td>
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the present time is its use for selection of patients with chronic internal carotid artery occlusion for bypass surgery. XeCT, on the other hand, is a reproducible quantitative technique that can be more easily used in the current clinical settings. It has classically been used for challenges like acetazolamide. The main limitation of XeCT is that Xenon is not currently approved by the FDA, and available at this time only under IND status. Doppler ultrasound is the easiest technique to perform at bedside and is consequently used in numerous institutions as the primary tool to assess brain hemodynamics. Its main drawback lies in the fact that it does not provide values for each brain region (but only one value for each supplying vessel or each hemisphere). To a certain extent, SPECT can also be performed at bedside: the radiopharmaceutical can be administered at the moment of the acute event, typically the seizure, and imaging is performed later, after stabilization of the patient, in order to identify the active epileptic focus. Among SPECT tracers, $^{133}$Xe is not only historically the most important method for measuring brain hemodynamics, but is still used as a gold standard in many hospitals that do not have PET. Doppler-ultrasound and ASL do not use any contrast medium and do not require radiation. They can be used repeatedly and, hence, are useful for intensive care monitoring (for Doppler ultrasound that can be performed at bedside) or functional imaging (for ASL). PCT technique can be performed on conventional CT scanners and, as such, represents an ideal technique for ED patients, including both stroke patients and head trauma patients. Finally, DSC can be combined with other MRI sequences, such as fine anatomic imaging, DWI, spectroscopy... in order to provide the most comprehensive information in one examination and leading to a high ratio benefit-cost.

As a conclusion, all imaging techniques dedicated to brain hemodynamics have their own advantages in specific clinical settings. The selection of one over another technique depends upon the intrinsic characteristics pertaining to each imaging technique, but also upon the settings and on the knowledge and experience of the institution's staff.

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[1] STEWART GN. Researches on the circulation time and on the influences which affect it. V. The circulation time of the spleen, kidney, intestine, heart (coronary circulation) and retina, with some further observations on the time of the lesser circulation. Am J Physiol 1921; 58: 278-295.


