Review

J. Neuroradiol., 2005, *32*, 294-314

COMPARATIVE OVERVIEW OF BRAIN PERFUSION IMAGING TECHNIQUES[1]

M. WINTERMARK [1, 2], M. SESAY [3], E. BARBIER [4], K. BORBÉLY [5], W.P. DILLON [1], J.D. EASTWOOD [6], T.C. GLENN [7], C.B. GRANDIN [8], S. PEDRAZA [9], J.F. SOUSTIEL [10], T. NARIAI [11], G. ZAHARCHUK [1], J.M. CAILLÉ [3], V. DOUSSET [3], H. YONAS [12]

(1) Department of Radiology, Neuroradiology Section, University of California, 505 Parnassus Avenue, Room L358, Box 0628, San Francisco, CA 94143-0628.

(2) Department of Radiology, University Hospital, Lausanne, Switzerland.

(3) Department of Neuroradiology, Pellegrin University Hospital, Bordeaux, France.

(4) Inserm, Université Joseph Fourier, UM 594, NeuroImagerie Fonctionnelle et Métabolique, CHU Michallon – Pav. B, Grenoble, France.

(5) Department of Nuclear Medicine, National Institute of Neurosurgery, Budapest, Hungary.

(6) Department of Neuroradiology, Duke University Medical Center, Durham, USA.

(7) Cerebral Blood Flow Laboratory and Brain Injury Research Center, Division of Neurosurgery, School of Medicine, UCLA Medical Center, Los Angeles.

(8) Department of Radiology, St Luc University Hospital, Université Catholique de Louvain, Brussels, Belgium.

(9) Radiology Department, IDI, Hospital Dr Josep Trueta, Girona, Spain.

(10) Department of Neurosurgery, Rambam Medical Center, The Technion, B. Rappaport Faculty of Medicine, Haifa, Israel.

(11) Department of Neurosurgery, Tokyo Medical and Dental University, Tokyo, Japan.

(12) Department of Neurosurgery, University of Pittsburgh, Pittsburgh, USA.

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 offers 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 Emission de Positrons (TEP), la Tomographie d'Emission 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

Reprint request: M. WINTERMARK, address (1) above.
e-mail: Max.Wintermark@radiology.ucsf.edu

[1]Reprinted with permission from *Stroke* (Wintermark M, Sesay M, Barbier E, Borbély K, Dillon WP, Eastwood JD *et al.* Comparative Overview of Brain Perfusion Imaging Techniques. *Stroke* 2005; 36: e83-e99). © 2005 American Heart Association, Inc.

brain hemodynamics in the form of parameters such as cerebral blood flow (CBF) or volume (CBV). They use different tracers (diffusible or non-diffusible, endogenous or exogenous) and have different technical requirements. Some are feasible at bedside, and others, not. The duration of data acquisition and processing varies from one technique to the other. Brain perfusion imaging techniques also differ by quantitative accuracy, brain coverage, and spatial resolution *(table I)*. These differences constitute as many advantages and drawbacks in various clinical settings.

The goal of this article is a comparative overview of the main brain hemodynamics imaging techniques, established by consensus among specialists of the different techniques. For clinicians, this should offer a clearer picture of the pros and cons of available brain hemodynamics imaging methods, and assist them in choosing the proper technique in every specific clinical setting. The different imaging techniques will be presented according to the same template. A technical description, including what kind of contrast is used and whether radiation is involved, 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 larges 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.

POSITRON EMISSION TOMOGRAPHY (PET) – *TADASHI NARIAI, KATALIN BORBÉLY*

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 ($rCMRO_2$), 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: $^{15}O_2$, $C^{15}O_2$, and $H_2{}^{15}O$. $H_2{}^{15}O$ 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]. $C^{15}O_2$ 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 $H_2{}^{15}O$; a 1-2min 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 $^{15}O_2$, $C^{15}O_2$ and $C^{15}O$ over 60 minutes allows to measure the rCBV, the $rCMRO_2$, 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: 1.7hrs,^{15}O: 2min, ^{13}N: 10min, ^{11}C: 20min). Whole-body radiation exposure by PET examination is usually 0.5 – 2.0mSv 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 $H_2{}^{15}O$ of or by 2) the continuous inhalation of $C^{15}O_2$. 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 $rCMRO_2$ 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