Intelligence in Medical Technologies

NeurInfarct

Dossier de presse

Press book

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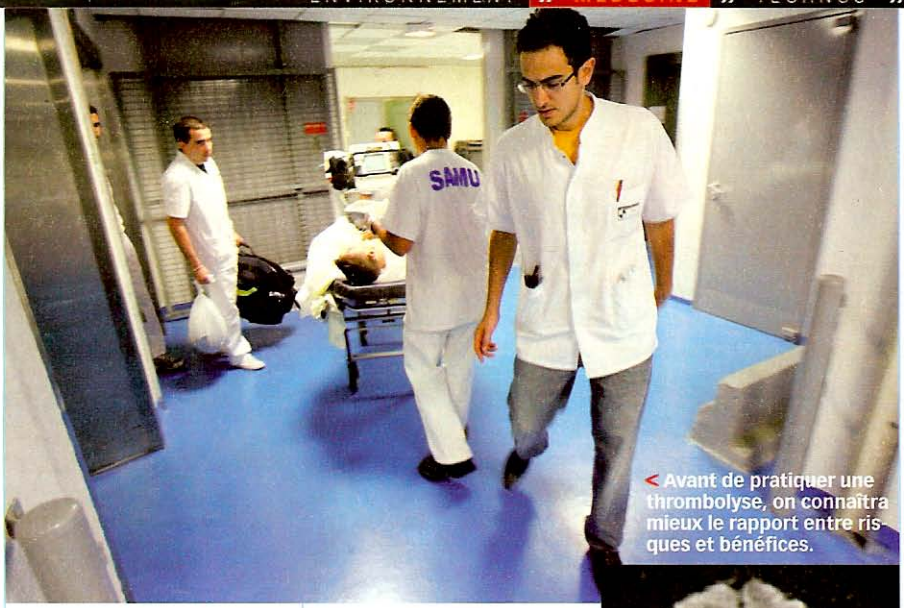
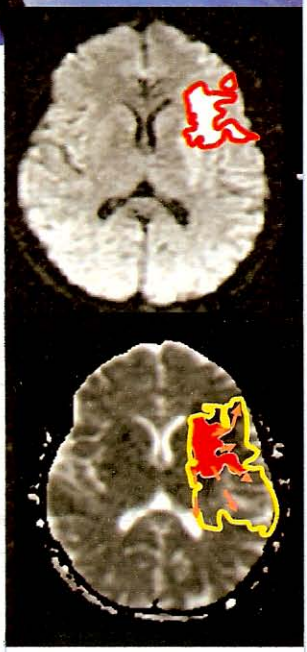


< Avant de pratiquer une thrombolyse, on connaîtra mieux le rapport entre risques et bénéfices.

NEUROLOGIE

On évalue mieux les dégâts d'un AVC sur le cerveau

Comment évaluer au plus vite l'étendue des dégâts potentiels sur le cerveau après un accident vasculaire cérébral (AVC)? En utilisant une nouvelle méthode d'imagerie cérébrale baptisée NeurInfarct, qui permet de visualiser la zone "sombre" potentiellement concernée par les lésions irréversibles. *Via* une IRM, la technique NeurInfarct détecte la présence d'eau à l'extérieur des cellules, un indicateur pertinent. Car lorsqu'elles sont en train de mourir, les cellules se gorgent d'eau, réduisant d'autant la présence d'eau autour d'elles. Ainsi, la zone "sombre" dans laquelle un processus de mort cellulaire s'est enclenché apparaît en clair sur l'image. "*Avec notre logiciel, la zone sombre devient visible*, explique Charlotte Rosso, neurologue à l'hôpital La Pitié-Salpêtrière, qui a collaboré à l'élaboration de cette nouvelle technique évaluée sur 100 patients. *Or cela permet de mieux évaluer le rapport entre le bénéfice et les risques encourus après une thrombolyse*". Très efficace, cette méthode consiste à injecter un produit en intraveineuse pour détruire le caillot… mais elle n'est pas sans risque! A tel point que la décision d'intervenir ou non s'apparente parfois à un casse-tête: elle dépend des résultats d'une IRM de perfusion, technique qui n'évalue pas la surface de la zone sombre. Et si la thombolyse réduit le risque de handicap (40 % de patients sans handicap après trois mois contre 26 % avec un placebo), elle peut provoquer des hémorragies graves dans 8 % des cas. **M.Cy.**



C.ROSSO, Y.SAMSON, D.DORMONT, S.BAILLET, CNRS, APHP, PITIÉ SALPÊTRIÈRE (2008) - I.HANNING/REA

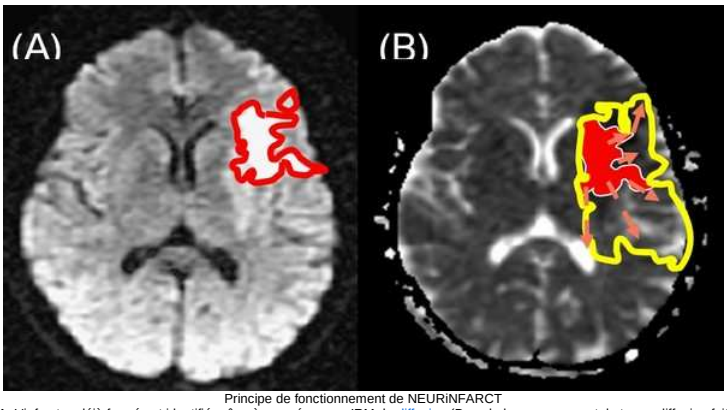
^ Avant, l'IRM n'isolait que la zone déjà morte (en haut). Désormais, la zone "sombre" devient visible (en jaune).

> FAITS & CHIFFRES

On dénombre **150 000 nouveaux cas d'AVC** par an en France et **1 personne sur 5 décède** dans le mois qui suit l'accident. Les **trois quarts** des survivants gardent des **séquelles** définitives.

NEURiNFARCT: prévoir l'évolution des accidents vasculaires cérébraux

Une nouvelle technique de prédiction de l'évolution des infarctus *(1)* cérébraux dans les premières heures (L'heure est une unité de mesure :) d'accidents vasculaires cérébraux (AVC) vient d'être évaluée sur près de 100 patients. Baptisée NEURiNFARCT, elle permet d'estimer l'étendue des tissus exposés au risque d'un infarctus en cours de formation chez un patient victime d'AVC grâce à une analyse inédite de mesures issues de l'imagerie par résonance (Lorsqu'on abandonne un système stable préalablement écarté de sa position d'équilibre, il y retourne, généralement à...) magnétique (IRM). Elle a été mise au point (Graphie) par une collaboration entre le Laboratoire de Neurosciences (Les neurosciences regroupent toutes les sciences nécessaires à l'étude de l'anatomie et du fonctionnement du système...) Cognitives & Imagerie Cérébrale *(2)* (CNRS), le département de Neuroradiologie et le service des Urgences Cérébro-Vasculaires du Groupe hospitalier Pitié-Salpêtrière (AP-HP). Les résultats, publiés en ligne sur le site de la revue *Radiology* dans l'article de Charlotte Rosso, neurologue affiliée à ce laboratoire montrent l'intérêt de cette technique novatrice pour prédire la gravité (La gravitation est une des quatre interactions fondamentales de la physique.) potentielle d'un infarctus en quelques minutes (Forme première d'un document : Droit : une minute est l'original d'un acte. ...), à partir d'images pouvant être obtenues sur un système IRM clinique conventionnel.



Principe de fonctionnement de NEURiNFARCT
A: L'infarctus déjà formé est identifié grâce à une séquence IRM de diffusion (Dans le langage courant, le terme diffusion fait référence à une notion de « distribution », de « mise à...) classique.
B: L'infarctus déjà formé est reporté sur la carte du coefficient (En mathématiques un coefficient est un facteur multiplicatif qui dépend d'un certain objet, comme une variable (par...) apparent de diffusion (dérivée automatiquement de l'IRM de diffusion originale).
NEURiNFARCT établit dès lors une prédiction automatique (L'automatique fait partie des sciences de l'ingénieur. Cette discipline traite de la modélisation, de l'analyse, de la...) du devenir de l'infarctus et de sa progression potentielle dans le cerveau du patient, ce qui permet au neurologue d'estimer le rapport bénéfice/risque des traitements agressifs existants pour limiter cette progression

NEURiNFARCT est une nouvelle méthode de détection de la "pénombre ischémique" qui est la zone de souffrance au sein de laquelle se développe dans les quelques heures qui suivent l'AVC, les lésions irréversibles de l'infarctus cérébral. Contrairement à l'infarctus, cette zone de pénombre reste viable et la sauver est l'objectif de la thrombolyse, traitement d'urgence de l'AVC qui réduit le risque de handicap, mais comporte un risque d'hémorragie secondaire. Les indications de ce traitement pourraient donc bénéficier d'une évaluation simple et rapide de l'étendue de cette zone de souffrance. Ceci a été l'enjeu des recherches à l'origine de NEURiNFARCT, les techniques IRM existantes restant relativement complexes à mettre en oeuvre et nécessitant l'injection (Le mot injection peut avoir plusieurs significations :) intraveineuse d'un produit de contraste. Cette dernière n'est plus nécessaire avec NEURiNFARCT qui repose uniquement sur des séquences IRM classiques. Ces images mesurent la mobilité des molécules d'eau (L'eau (que l'on peut aussi appeler oxyde de dihydrogène, hydroxyde d'hydrogène ou acide hydroxyque) est un...) qui est très diminuée au coeur de l'infarctus, mais qui est également légèrement perturbée dans la zone de pénombre. Ces dernières altérations sont trop discrètes pour être visibles à l'oeil nu sur les images et la difficulté consista à développer un outil (Un outil est un objet finalisé utilisé par un être vivant dans le but d'augmenter son efficacité naturelle dans...) d'analyse automatique, basé sur un modèle simulant la croissance réelle de l'infarctus. Les résultats publiés dans Radiology indiquent que les performances obtenues par NEURiNFARCT sont au moins aussi bonnes que celles des méthodes qui utilisent l'imagerie de perfusion en IRM ou en scanner (Un scanneur, ou numériseur à balayage est l'équivalent du terme anglais scanner, qui vient du verbe anglais to scan,...) et qui nécessitent l'injection intraveineuse de produits de contraste. En outre, contrairement à l'imagerie de perfusion, les résultats obtenus avec NEURiNFARCT sont fiables et standardisés car la méthode est quasi-entièrement automatique, ce qui est un avantage certain dans le contexte (Étape →3/5 : Une relecture a été demandée. • Si vous voyez des erreurs de traduction, vous pouvez...) clinique d'extrême urgence de l'AVC.

Cette approche pourrait constituer un outil essentiel d'aide à la décision thérapeutique en urgence et d'évaluation rapide de nouveaux traitements pour l'industrie pharmaceutique. Le logiciel (Un logiciel ou une application est un ensemble de programmes, qui permet à un ordinateur ou à un système informatique...) résultant est actuellement utilisé dans des protocoles de recherche (La recherche scientifique désigne en premier lieu l'ensemble des actions entreprises en vue de produire et de...) clinique dans le but d'évaluer plus efficacement de nouvelles approches thérapeutiques contre les infarctus cérébraux en formation.

Les enjeux sont de taille quand on sait que les personnes handicapées à la suite d'un AVC sont aujourd'hui aussi nombreuses en France que celles atteintes des maladies d'Alzheimer et de Parkinson. La technique NEURiNFARCT, issue d'une collaboration avec les neurologues du service des Urgences Cérébro-Vasculaires *(3)* du Service de Neuroradiologie de l'hôpital de la Salpêtrière, a fait l'objet d'un brevet international et sa valorisation est envisagée.

Notes:

(1) Nécrose d'un organe résultant de l'obstruction de l'artère qui assure son irrigation (L'irrigation est l'opération consistant à apporter artificiellement de l'eau à des végétaux cultivés pour...).
(2) (LENA), équipe Modélisation et Méthodologie en Imagerie Cérébrale dirigée par Sylvain Baillet.
(3) Du Pr Yves Samson et du Pr Didier Dormont.

NEURiNFARCT, une nouvelle technique d'IRM permet de prévoir l'évolution des accidents vasculaires cérébraux 30-11-2008 - Une nouvelle technique de prédiction de l'évolution des infarctus (1) cérébraux dans les premières heures d'accidents vasculaires cérébraux (AVC) vient d'être évaluée sur près de 100 patients.

Baptisée NEURiNFARCT, elle permet d'estimer l'étendue des tissus exposés au risque d'un infarctus en cours de formation chez un patient victime d'AVC grâce à une analyse inédite de mesures issues de l'imagerie par résonance magnétique (IRM).

Elle a été mise au point par une collaboration entre le Laboratoire de Neurosciences Cognitives & Imagerie Cérébrale (2) (CNRS), le département de Neuroradiologie et le service des Urgences Cérébro-Vasculaires du Groupe hospitalier Pitié-Salpêtrière (AP-HP). Les résultats, publiés en ligne sur le site de la revue Radiology dans l'article de Charlotte Rosso, neurologue affiliée à ce laboratoire montrent l'intérêt de cette technique novatrice pour prédire la gravité potentielle d'un infarctus en quelques minutes, à partir d'images pouvant être obtenues sur un système IRM clinique conventionnel.

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Laetitia Louis

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MÉTHODE D'ESTIMATION DU POTENTIEL DE CROISSANCE DES INFARCTUS CÉRÉBRAUX

L'invention concerne une méthode d'estimation automatique du potentiel de croissance des infarctus cérébraux en particulier en phase aiguë, c'est-à-dire dans les six heures suivant la survenue de l'accident ischémique cérébral.

À ce titre, l'invention concerne le domaine de l'imagerie cérébrale et plus particulièrement l'analyse et le traitement d'images obtenues par résonance magnétique (IRM) pour déterminer le potentiel de croissance des infarctus cérébraux durant leur phase aiguë. L'intérêt de cette démarche est de déterminer de façon précoce le rapport bénéfices/risques que présente la mise en œuvre de traitements, efficaces mais agressifs, pour lutter contre la propagation de ces accidents vasculaires cérébraux.

Il est connu de l'état de la technique quelques méthodes utilisées sous forme d'outils logiciels non encore standardisés. Les méthodes actuelles de prédiction de croissance des infarctus cérébraux à partir de données d'imagerie sont essentiellement basées sur la comparaison des anomalies des séquences IRM de perfusion et de diffusion, ou sur l'étude des images issues du scanner de perfusion.

À ce titre, la demande de brevet internationale n° WO 07/058632 décrit les différentes étapes permettant d'obtenir une estimation du potentiel de croissance de l'infarctus, selon de telles méthodes. Malgré leur intérêt théorique majeur, toutes ces méthodes se sont heurtées à des limitations physiopathologiques et méthodologiques diverses. Leur standardisation s'est révélée extrêmement complexe et aucune d'entre elles ne s'est imposée comme un standard incontournable. De ce fait, leur mise en œuvre reste confinée au cadre de la recherche physiopathologique ou éventuellement à celui d'essais thérapeutiques à grande échelle auxquels ne peuvent participer que quelques centres hautement spécialisés.

Computer Assisted Radiology and Surgery

Automatic Prediction of Infarct Growth in Acute Ischemic Stroke from MR Apparent Diffusion Coefficient Maps[1]

Nidiyare Hevia Montiel, Charlotte Rosso, Narie Chupin, Sanorine Deltour, Eric Bardinet, Didier Dormont
Yves Samson, Sylvain Baillet

Rationale and Objectives. We introduce a new approach to the prediction of final infarct growth in human acute ischemic stroke based on image analysis of the apparent diffusion coefficient (ADC) maps obtained from magnetic resonance imaging. Evidence from multiple previous studies indicate that ADC maps are likely to reveal brain regions belonging to the ischemic penumbra, that is, areas that may be at risk of infarction in the few hours following stroke onset.

Materials and Methods. In a context where "time is brain," and contrarily to the alternative—and still-debated—perfusion-diffusion weighted image (PWI/DWI) mismatch approach, the DWI magnetic resonance sequences are standardized, fast to acquire, and do not necessitate injection of a contrast agent. The image analysis approach presented here consists of the segmentation of the ischemic penumbra using a fast three-dimensional region-growing technique that mimics the growth of the infarct lesion during acute stroke.

Results. The method was evaluated with both numerical simulations and on two groups of 20 ischemic stroke patients (40 patients total). The first group of patient data was used to adjust the parameters of the model ruling the region-growing procedure. The second group of patient data was dedicated to evaluation purposes only, with no subsequent adjustment of the free parameters of the image-analysis procedure. Results indicate that the predicted final infarct volumes are significantly correlated with the true final lesion volumes as revealed by follow-up measurements from DWI sequences.

Conclusion. The DWI-ADC mismatch method is an encouraging fast alternative to the PWI-DWI mismatch approach to evaluate the likeliness of infarct growth during the acute stage of ischemic stroke.

Key Words. Stroke; magnetic resonance imaging; diffusion imaging; region-growing segmentation; cerebral ischemia; infarct growth prediction; apparent diffusion coefficient.

In the immediate aftermath of acute ischemic stroke, estimation of the significant growth potential of radiologic abnormalities detected during the early therapeutic window is critical. In the context of the acute phase of ischemic stroke, neurologists consider that the patient outcome is ruled by a "time is brain" conception. The vascular system of the brain is segregated into a limited number of territories dedicated to blood supply. Consequently, depending on the initial locus of the occlusion within the vascular system, specific regions of the ipsilateral hemisphere will be at risk of subsequent infarct. Therefore after the initial extent of the early infarct has been identified, the neurologist needs to evaluate the functional territory at risk to anticipate any potential future functional impairment for the patient. Indeed, the final volume of the infarct—which may initially be rather small in the acute phase but might grow dramatically in the next few hours—is a central evaluation factor of stroke patients.

Acad Radiol 2008; 15:77–83

[1] From the Cognitive Neuroscience & Brain Imaging Laboratory (N.H.M., C.R., E.B., D.D., S.B.), Brain Stroke Emergency Unit (C.R., S.D., Y.S.), Neuroradiology Department, (D.D.), CNRS UPR640-LENA; Pierre & Marie Curie University, Paris 6; La Salpêtrière Hospital; Paris, France. Received January 2, 2007; accepted July 13, 2007. Supported in part by the CONACYT program for graduate training from the Mexican Ministry of Research and the SFERE graduate program from the French Ministry of Research. **Address correspondence to:** S.B. e-mail: sylvain.baillet@chups.jussieu.fr

doi:10.1016/j.acra.2007.07.007

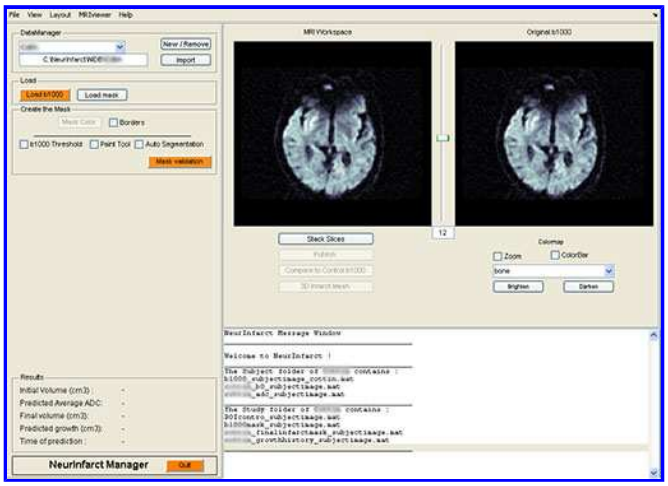
NEURiNFARCT

Fast prediction of infarct growth

from diffusion weighted MRI imaging during acute stroke

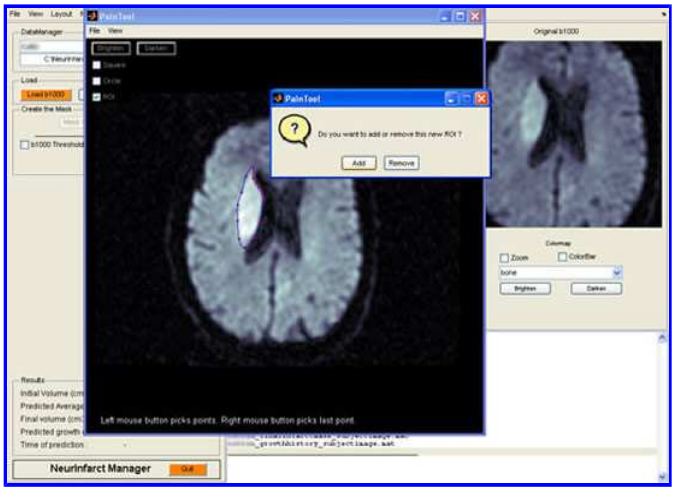
The core methodology of **NEURiNFARCT** consists of the prediction of infarct growth from MR-DWI data acquired during the acute stage of stroke.Our basic research has demonstrated that the non invasive prediction in the acute stage of the final growth of the ischemic lesion would reach very good agreement with retrospective measures.

NEURiNFARCT is a software prototype developed in our group under Matlab. The software workflow was designed following to clinical standards and is highly interactive its graphical user interface.

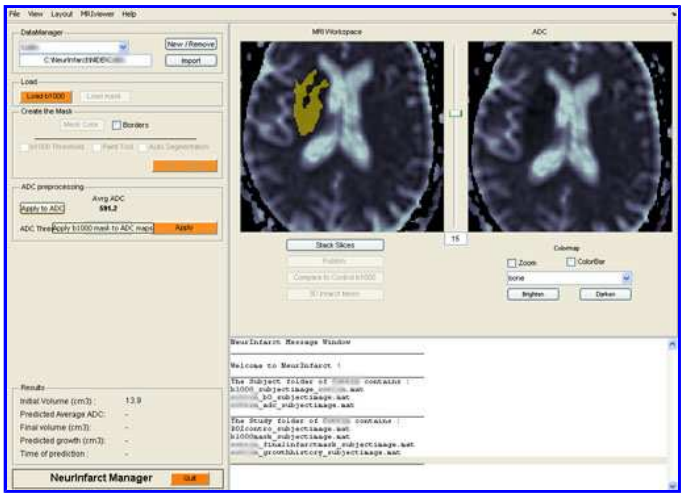


The workflow consists of 3 consecutive steps:

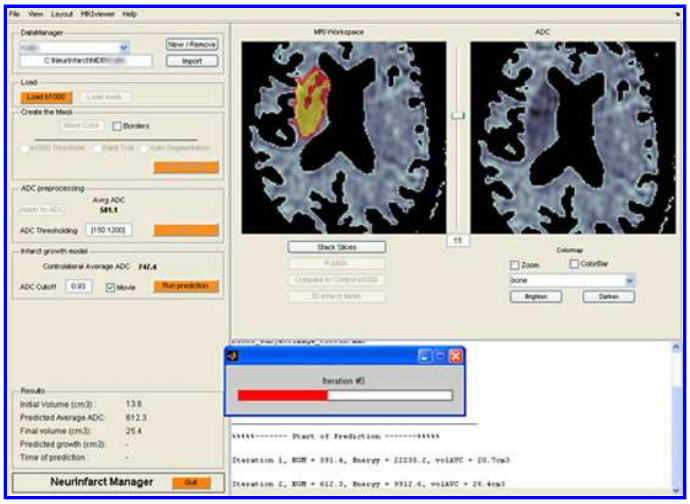
1) Segmentation of the initial lesion using a large palette of automatic/manually-assisted tools.



2) Registration of the initial mask of the initial lesion to ADC maps.



3) Prediction of final lesion using a region-growing infarct model.



Growth prediction follows an iterative process which is updated in real time and therefore, can be controlled by the clinical expert. The final characteristics of the ischemic lesion (location, volume, ADC statistics, etc.) are summarized in a report sheet which includes visualization of the estimate of the final lesion using 2D image stacks, or even 3D renderings.

See video of prediction

NEURiNFARCT has been developed as a software prototype and is now available for collaborative evaluation and testing at a larger scale. The usage of the tool has been documented and can be proficiently comprehended by clinical neurologists and radiologists with minimum training. Please contact us is you are interested in trying out **NEURiNFARCT**!

"Method of Predicting Stroke Evolution Utilising MRI"

THIS INVENTION relates to a method for predicting infarct evolution using magnetic resonance imaging (MRI) and image processing. In particular, the invention is directed to an automated method for estimating the volume of dead nervous tissue resulting from a stroke, using imaging information obtained shortly after the onset of stroke symptoms.

BACKGROUND ART

Typically, a person suffers an ischemic infarction or stroke when a blood vessel is blocked, causing cerebral nervous tissue to be deprived of oxygen. In the initial few hours after a stroke, there is usually a significantly reduced blood supply to a region of nervous tissue due to a blocked or nearly-blocked blood vessel which would otherwise supply oxygen to that tissue. The nervous tissue deprived of adequate blood supply does not necessarily die immediately. It can often die over the next 18 hours or so. The prediction of the final size of the stroke, i.e. the final volume of dead tissue is very difficult.

If the stroke evolution is known, the patient can receive appropriate treatment. For example, if the stroke is expected to evolve into a significant volume of dead nervous tissue, the patient can be placed in intensive care and/or administered strong medication in an effort to minimise the effects of the stroke. Alternatively, if the stroke is not expected to evolve further, the patient may be given less intensive therapy, and avoid the side effects associated with the powerful drugs. An ability to predict or estimate stroke evolution would therefore be a highly beneficial and useful tool in the treatment of stroke patients.

Known methods of stroke evaluation generally rely on the use of subjective measures such as operator defined regions of interest on diffusion and perfusion maps to enable prediction of infarct size. However, these methods are time consuming to implement and require highly skilled practitioners. Further, there is a limited time window of opportunity for the administration of thrombolytic or neuroprotective therapy. Thus a basic criterion

Automatic prediction of infarct growth in acute ischemic stroke from MR apparent diffusion coefficient maps

N. Hevia Montiel[a] · C. Rosso[a,b] · M. Chupin[a] · S. Deltour[b] · E. Bardinet[a] · D. Dormont[a,c] · Y. Samson[b] · S. Baillet[a]

[a]Cognitive Neuroscience & Brain Imaging Laboratory, CNRS UPR640-LENA; AP-HP, La Salpêtrière Hospital; Pierre & Marie Curie University, Paris, France

[b]AP-HP; Brain Stroke Emergency Unit, La Salpêtrière Hospital, Paris, France

[c]AP-HP; Neuroradiology Department, La Salpêtrière Hospital, Paris, France

Abstract We introduce a new approach to the prediction of the final infarct growth in human acute ischemic stroke based on image analysis of the apparent diffusion coefficient (ADC) MR maps acquired in the acute stage The ADC maps are likely to reveal brain regions belonging to the ischemic penumbra, that is, areas that may be affected by the infarction in the following next few hours. In a context where "time is brain", and contrarily to the most developed—though still-debated—perfusion–diffusion mismatch approach, the ADC MR sequences are fast to acquire and do not necessitate injection of a contrast agent. Image analysis consists of the segmentation of the ischemic penumbra using a fast 3D region-growing infarct approach.

Keywords Stroke · Magnetic resonance imaging · Diffusion imaging · Region-growing segmentation · Cerebral ischemia · Infarct growth prediction · Apparent diffusion coefficient

1 Introduction

In the immediate aftermath of acute ischemic stroke, knowledge on the significant growth potential of radiological abnormalities detected during the early therapeutic window is of critical importance. Prediction of the regions—and consequently functional systems—eventually involved in the infarct will influence the very choice of the most effective therapy. In this context, recent MR sequences could contribute to reduce the huge social impact of stroke if image analysis tools for accurate and immediate distinction between the already-infarcted and still-at-risk ischemic tissues can be provided. A first approach consists in determining thresholds on imaging measures to distinguish between regions (1) bound to spontaneous recovery, (2) threatened but potentially viable, the ischemic penumbra or, (3) irreversibly injured and infarcted [12]. The penumbra region is an assembly of areas that may be affected by the infarction in the following next few hours. It includes functionally impaired but

salvageable ischemic brain tissue surrounding an irreversibly damaged core.

Like in other non-ischemic CNS pathologies, basic structural MRI can help reveal the earliest hemodynamic and a tissue change induced by ischemia [4], but carries no information about the forthcoming outcome of the infarct growth. In this context, the perfusion–diffusion mismatch approach has been proposed to estimate the growth potential of the infarct in the acute phase, with limited specificity though [1, 11]. Alternatives based on diffusion MR imaging such as diffusion-weighted (DWI) and apparent diffusion coefficient (ADC) maps may unveil three types of information: the initial location of the early cerebral ischemic accident; the final volume of abnormalities with irreversible lesions at the time the MRI scan was acquired; and the severity of ischemia. Because of the advent of these techniques in clinical MRI units, recent studies have highlighted the clinical value of DWI in stroke diagnosis and the potential impact of water ADC measurement on the quantification and prediction of histopathologic damage in ischemic brain infarcts [7, 8, 9]. DWI for instance, reveals relative hypersignals in regions with lower diffusion, such as areas of acute stroke. Tissues in which water diffusion is reduced can therefore be readily detected as a hyperintense area on heavily diffusion-weighted MR images, which has become the hallmark of detection of recent ischemic stroke. These signal discrepancies also correspond to reduced water ADC in ischemic brain tissue due to cytotoxic oedema [3]. The smaller ADC values in the vicinity of the early-infarcted core are also indicative of tissue at risk of final infarction. Indeed, subtle ADC changes remain invisible on DWI, and early moderate decrease in ADC may occur in true penumbra. Extraction of the penumbra area from ADC maps within 6 h following stroke onset could help predict the infarct growth and, even more accurately, the final size of the infarct [4, 8, 10]. Further, DWI signal intensity depends on multiple factors such as the diffusion rate of molecules, T1 and T2 relaxation times, and local proton density. ADC, however, is independent of confounding T2 effects and ADC average or ''trace'' maps are also independent of diffusion anisotropy. Finally, ADC is an absolute measure expressed in $mm^2\ s^{-1}$, which is independent on the scanner [2].

2 Subjects and methods

The present study consisted of the development and pilot evaluation of a region growing segmentation technique of ADC maps dedicated to the extraction of brain areas likely to be affected by infarct within the next few days following stroke.

2.1 Patients

The patient population consisted of an initial database of 20 patients (age: mean 57, range [30, 73]; 100% without re-permeability) to tune the parameters of the method and a larger database of 77 patients (age: mean 59, range [26, 84]; with 49% complete, 22% partial, 29% without re-permeability) dedicated to its evaluation. These patients suffered from acute hemispheric stroke and were scanned with DWI within the 6 first hours following symptoms onset. ADC maps were obtained from DWI processing. A follow-up scan was performed within the next 1.2 days on average (range [0.5, 6.3]).

2.2 Imaging parameters

DWI scans consisted of 24 256×256 axial slices (5 mm thickness) with an inter-slice gap of 0.5 mm. Each axial slice was obtained with spin-echo multi-slice single-shot echo-planar imaging sequence with a baseline T2 acquisition (b = 0 s mm^{-2}) and b = 1,000 s mm^{-2}. ADC ''trace'' images were generated with a dedicated software tool (FuncTool, General Electric, Buc, France).

2.3 Image pre-processing

Original image processing tools were developed in C on a conventional Linux workstation under the brainVISA environment (http://www.brainvisa.info). Initial and follow-up scans were co-registered in the Talairach reference system and retrospective quantitative measurements were obtained from three pathophysiological regions of interests (ROI): (1) the volume of initial DWI abnormalities, which was considered as the ischemic core (CORE); (2) the final volume of the infarct (INF) taken from the final DWI abnormalities; and (3) the at-risk region or infarct growth area (IG), defined as the difference between INF and CORE ROIs. Mirror regions were also delineated for subsequent comparison with ADC values within contralateral healthy tissues. ADC maps were thresholded between 150 and 1,200 $mm^2\ s^{-1}$ to remove voxels contaminated with partial volume effects from cerebrospinal fluid. For each patient, all ROIs were manually delineated by the neurologist for quantitative comparison with the outcomes of the automatic segmentation procedure.

2.4 Image analysis and region-growing segmentation

The segmentation procedure is guided by a region-growing process as a modelling approach to the infarct growth. Initialization consists of the definition of a mask for the initial lesion obtained by expert neurologists using visual adaptive thresholding of the initial DWI (see [5] for automatic alternatives). Growth then runs through iterative voxel classification at the evolving infarct 3D envelope using voxel-based and region-based prior models of ADC intensity profiles in the INF region. These models are built on basic sample statistics of ADC values that were extracted from all ipsi and contralateral ROIs in the initial database (Table 1). Voxel classification is therefore achieved by alternatively considering the next voxel candidates as either ultimately belonging to the final infarct region or to healthy tissue. The numerical objective consists in minimizing a global energy index E computed over the set of voxels v in the INF region. Recent studies have demonstrated that the average and individual voxel ADC intensity values are significantly smaller in the INF region during the acute stage than in controlateral healthy tissues [6,11]. Therefore, E includes terms that relate to region and pixel-based properties (E_R and E_P, respectively) of the infarct volume and a regularizing feature, E_s, which ensures a smooth surface envelope to the infarct volume along iterations: $E = \alpha E_R + \beta E_P + \gamma E_S$. α, β and γ are scalar hyperparameters. The individual energy terms are defined as:

Table 1 Sample statistics of ADC intensity values obtained from the initial database ($N = 20$): region-based (average ADC values and standard deviations for each ROI) and voxel-based statistics (sample statistics of the voxel population in each ROI)

	ADC intensities					
	Region-based statistics			Voxel-based statistics		
ROI	CORE	IG	INF	CORE	IG	INF
Lesion	645 ± 75	823 ± 43	750 ± 69	690 ± 199	824 ± 174	772 ± 196
Mirror	840 ± 52	860 ± 36	851 ± 44	851 ± 167	860 ± 160	861 ± 156
Ratio	0.77	0.96	0.88	0.81	0.96	0.90

The mean ADC values of regions can further be compared with the values in the contralateral healthy hemisphere and expressed as an ADC ratio

$$E_R = \left(\frac{\bar{i}_{INF} - i_{INF}}{\sigma_{INF}}\right)^2, \text{ where } \bar{i}_{INF} = \frac{1}{N_{INF}} \sum_{v \in INF} i(v);$$

$$E_P = \sum_{v \in IG} \left(\frac{i(v) - i_{IG}}{\sigma_{IG}}\right)^2; \quad E_S = \sum_{v \in INF} \left(\frac{N_v - N/2}{\delta}\right)^\beta.$$

All voxel intensity values in E_R and E_P are expressed relatively to the average tissue intensity in the contralateral healthy region (see Sect. 3). $\bar{i}_{INF}$ is the average ADC intensity in the current INF region; i_{INF} (res. σ_{INF}) is a prior on the expected average (res. tolerance) ADC intensity in the final INF region. $i(v)$ is the ADC intensity at voxel v. $\bar{i}_{IG}$ (res. σ_{IG}) is also a prior on the expected ADC intensity (res. standard deviation) at the voxel level for voxels in IG. N_{INF} (res. N_{IG}) are the current counts of voxels in the INF and IG regions, respectively. E_S is the Ising regularization functional: N is the total number of

voxel neighbours (e.g. 26) out of which N_v belong to INF. δ and β are fixed scalar parameters. Global optimization is run iteratively on each element v_0 of the voxel front according to: $v_0 \in \text{INF} \Leftrightarrow E_{v_0 \in \text{INF}} < E_{v_0 \notin \text{INF}}$. Growth is complete when no more voxels are acceptable in the INF region. Infarct growth was considered as significant if the IG volume was superior to 10 cm^3. Performances of our method were then evaluated in terms of specificity and sensitivity of infarct growth prediction and compared with those generally observed from the perfusion–diffusion mismatch alternative approach.

3 Results

The average volume of the infarct lesions in the initial database increased from 36 ± 26 cm^3 (CORE) to 96 ± 81 cm^3 (INF). In the hemisphere ipsilateral to the infarct, ADC intensity values revealed significant differences between all 3 ROI types, while as expected, no difference were detected between the corresponding mirror ROIs in the healthy hemisphere (Table 1). Our study confirms that average ADC values are significantly smaller in CORE than in INF [10].

In the final evaluation database (N = 77), the volume of the lesion increased from 40 ± 36 cm^3 to 81 ± 72 cm^3, (mean growth: 41 ± 50 cm^3). The average final infarct volume predicted by our method was 79 ± 72 cm^3, with significant correlation with the true final volumes (resp. infarct growth) at the population level: r = 0.71 (resp. r = 0.56; Fig. 1a), $P < 0.0001$.

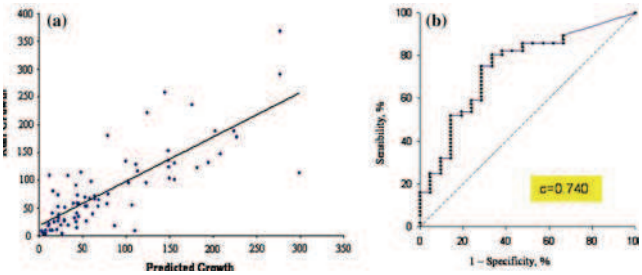


Fig. 1 **a** Real vs. predicted infract growth volumes. **b** ROC analysis of the performances from the automatic prediction method. **c** Area under the curve

Automatic prediction of the infarct growth performed with 75% sensitivity and 71% specificity scores. ROC analysis revealed a satisfactory measure of the area under the curve index (c = 0.74, Fig. 1b). These performances are comparable to the ones achieved by the perfusion–diffusion mismatch approach, though this latter necessitates the monitored injection of a contrast agent in the scanner, a heavy constraint in the context of absolute emergency. Convergence of the iterative algorithm was fast (< 10 min on average, on a conventional workstation). The method is exemplified Fig. 2.

4 Conclusions

Because the ADC values reflect the ischemic history of the tissue, this parameter was confirmed to be predictive of final tissue outcome. We have shown in this study that automatic segmentation of the ADC profile from early scans is reliable, fast, and no-invasive. Segmentation was achieved by a region-growing procedure that includes limited a priori knowledge about the infarcted area: the expected average ADC value—derived from the retrospective analysis on a limited population of patients—and smooth surface envelopes priors. These are encouraging results for the fast and automatic segmentation of ADC maps in the anticipation of infarct growth and represent an alternative to the still-debated perfusion–diffusion mismatch approach. Ongoing research includes refinement of the segmentation procedure to achieve greater quantitative accuracy by including extended knowledge on brain vascular structure and comprehensive investigation of the 3D ADC profile.

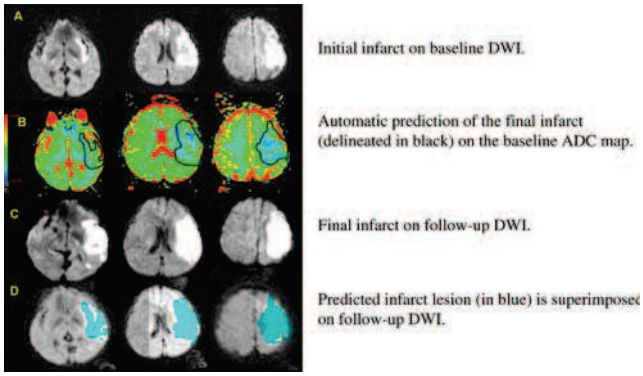


Fig. 2 An example of the automatic prediction in a patient with initial infarct volume of 81.9 cm^3 (**a**), the real final infarct volume is 130.4 cm^3 (**c**), and the predicted final volume was 154.9 cm^3 (**b**, **d** with blue mask). True (resp. predicted) growth is 48.5 cm^3 (resp. 68.0 cm^3)

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Prediction of Infarct Growth Based on Apparent Diffusion Coefficients: Penumbral Assessment without Intravenous Contrast Material

Appendix E1

We present here a technical summary of the image processing method for estimating the final extent of the infarct lesion from acute diffusion-weighted MR image series.

The segmentation procedure per se consists of an isotropic region-growing process as a modeling approach to infarct growth. Image segmentation models using region-growing techniques have proved to be efficient in multiple-image-analysis problems in which target objects have ill-defined boundaries, as in the present context of delineating the infarct penumbra. Before performing the region-growing image analysis on ADC image maps, the latter were first thresholded between 150 and 1200 $mm^2 \cdot sec^{-1}$ to remove voxels contaminated with partial-volume effects from, for example, cerebrospinal fluid. The growth model mimics the putative natural history of infarct growth and is initiated from the mask of the admission infarct zone obtained from thresholding of the baseline diffusion-weighted images by an expert neurologist. The algorithm then proceeds by successive accumulation of voxels with use of voxel-based and region-based prior models of ADC intensity profiles within the penumbral region: (*a*) A regional constraint compares the running average ADC value within the growing infarct (regional ADC) to a predefined target value; (*b*) a local constraint prevents voxels with unexpectedly high ADC values from being included in the infarct (local ADC); and (*c*) a regularity constraint that ensures a smooth shape to the infarct, as expected from physiology.

Voxel classification is iterative and proceeds as follows. At every iteration, all voxel candidates at the leading edge of region growth are considered as ultimately either belonging to the final infarct region or to healthy tissue. The numeric objective consists of minimizing a global energy index E computed over the set of voxels v previously classified as members of the final infarct region. E consists of three terms, one for each of the above-mentioned constraints and which relate to region- and voxel-based properties (E_R and E_V, respectively) of the infarct volume and a regularizing feature E_C, which ensures a smooth surface

Prediction of Infarct Growth Based on Apparent Diffusion Coefficients: Penumbral Assessment without Intravenous Contrast Material[1]

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Didier Dormont, MD, PhD
Sophie Crozier, MD
Sylvain Baillet, PhD
Yves Samson, MD

Purpose: To compare predicted and final infarct lesion volumes determined by processing apparent diffusion coefficient (ADC) maps derived at admission diffusion-weighted (DW) magnetic resonance (MR) imaging in patients with acute stroke and to verify that predicted areas of infarct growth reflect at-risk penumbral regions based on recanalization status.

Materials and Methods: The French legislation waived the requirement for informed patient consent for the described research, which was based on patient medical files. However, patients and/or their relatives were informed that they could decline to participate in the research. Authors tested a semiautomated proprietary image analysis procedure in 98 patients with middle cerebral artery (MCA) stroke by modeling infarct growth on DW imaging–derived ADC maps. Predicted infarct growth (PIG) areas and predicted infarct volumes were correlated with final observed data. In addition, the effect of MCA recanalization on the correlation between predicted and observed infarct growth volumes was qualitatively assessed.

Results: Predicted and final infarct volumes ($\rho = 0.828$; 95% confidence interval [CI]: 0.753, 0.882; $P < .0001$) and infarct growth volumes ($\rho = 0.506$; 95% CI: 0.342, 0.640; $P < .0001$) were significantly correlated. Visual comparative examination revealed satisfactory qualitative consistency between predicted and follow-up lesion masks. In patients without MCA recanalization, PIG did not differ significantly from final observed infarct growth (median PIG obtained with 0.93 ADC ratio cutoff [PIG_{ratio}] of 27.1 cm^3 vs median infarct growth of 19.8 cm^3, $P = .17$). MCA recanalization revealed an overestimation of PIG (median PIG_{ratio} of 24.8 cm^3 vs median infarct growth of 12 cm^3, $P = .005$), suggesting that the PIG area was part of ischemic penumbra.

Conclusion: Data show the feasibility of identifying at-risk ischemic tissue in patients with acute MCA stroke by using semiautomated analysis of ADC maps derived at DW imaging, without intravenous contrast material–enhanced perfusion-weighted imaging.

Supplemental material: *http://radiology.rsnajnls.org/cgi/content/full/2493080107/DC1*

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A new MRI technique allows for the development of stroke

Tagged with: acute stroke, conventional clinical, MRI sequences, MRI technique, NEURiNFARCT, Radiology, thrombolysis
Thursday, November 27, 2008, 7:11
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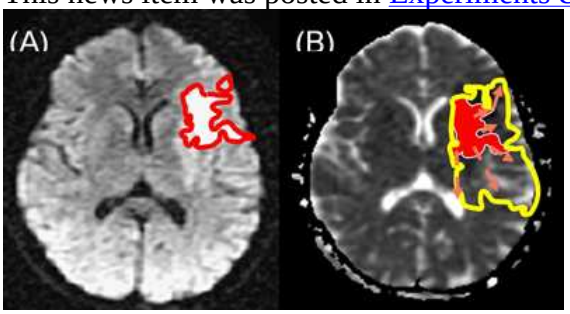


Operating principle of NEURiNFARCT.

A new technique for predicting the evolution of infarction (1) brain in the early hours of stroke (AVC) has been evaluated nearly 100 patients. Dubbed NEURiNFARCT, it allows to estimate the extent of tissue at risk of a heart attack during training in a patient victim of stroke through an analysis of new measures from magnetic resonance imaging (MRI). It was developed through collaboration between the Laboratory of Cognitive Neuroscience and Brain Imaging (2) (CNRS), the Department of Neuroradiology and emergency department Cerebro-Vascular Group Hospitalier Pitié-Salpêtrière (AP-HP). The results, published online on the site of the journal Radiology in the article by Charlotte Rosso, neurologist affiliated with this laboratory show the value of this innovative technique to predict the potential severity of a heart attack within a few minutes out from images can be obtained on a conventional clinical MRI system.

NEURiNFARCT is a new method for detecting the “ischemic penumbra” which is the area of pain in which develops within a few hours after the stroke, irreversible damage to cerebral infarction. Unlike infarction, this twilight zone remains viable and rescue is the objective of thrombolysis treatment of acute stroke that reduces the risk of disability, but carries a risk of bleeding secondary. The indications for this treatment could benefit from a simple and rapid assessment of the extent of this zone of suffering. This was the challenge to research the origin of NEURiNFARCT, existing MRI techniques still relatively complex to implement and requires intravenous injection of contrast. The latter is no longer necessary with NEURiNFARCT based solely on conventional MRI sequences. These images measure the movement of water molecules that is very much diminished in the heart of heart, but also slightly disturbed in the twilight zone. These recent changes are too discrete to be visible to the naked eye on the images and the challenge is to develop a tool for automatic analysis, based on a model simulating real growth infarction. The results published in Radiology indicate that the performance by NEURiNFARCT are at least as good as those methods that use perfusion imaging or MRI scanner and require intravenous injection of contrast. In addition, unlike the perfusion imaging, the results are reliable and NEURiNFARCT standardized because the method is almost entirely automatic, which is an advantage in the clinical context of extreme urgency of stroke.

This approach could be an essential tool for decision support therapeutic and emergency rapid assessment of new treatments for the pharmaceutical industry. The resulting software is currently used in clinical research protocols in order to more effectively evaluate new therapeutic approaches against the cerebral infarction in training.

The stakes are high when we know that people with disabilities following a stroke are as numerous

as those in France suffering of Alzheimer's and Parkinson's. The technique NEURiNFARCT, after a collaboration with neurologists Emergency Service Cerebro-Vascular (3) Neuroradiology Service of the Hospital de la Salpêtrière, has been the subject of an international patent and its recovery is considered.

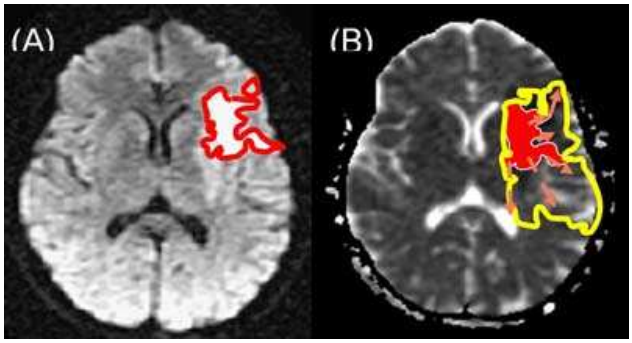
Notes:

(1) necrosis of an organ resulting from obstruction of the artery that provides its irrigation.
(2) (LENA), Modeling and Methodology team in brain imaging directed by Sylvain Baillet.
(3) Professor Yves Samson and Professor Didier Dormont.
References:

C. ROSSO, N. HEVIA-Montiel, S. DELTOUR, E. Bardinet, D. DORMONT, S. CROZIER, S. BAILLET, and Y. SAMSON. PREDICTION OF GROWTH BASED ON Infarcts apparent diffusion coefficient: PENUMBRAL ASSESSMENT WITHOUT intravenous CONTRAST. RADIOLOGY PUBLISHED IN LINE ON THE SITE OF RADIOLOGY, NOVEMBER 18, 2008.

NEURiNFARCT for Predicting Cerebral Infarct Development

Filed under: in the news...



Using an MRI machine French scientists were able to predict the evolution of cerebral infarcts in stroke patients. The collaboration involved researchers from the Cognitive Neuroscience & Brain Imaging Laboratory of the French National Center for Scientific Research (CNRS) and the Neuroradiology Department and the Acute Stroke Centre of the Pitié-Salpêtrière General Hospital in Paris, France.

NEURiNFARCT is a new technique for the identification of the "ischemic penumbra", a region which is rapidly developing within the next few hours after stroke onset and may conduct to severe irreversible brain lesions. Contrarily to the zone of initial infarct, the penumbra region may be saved during the early acute phase of stroke – and therefore the risk of subsequent deficits for the patients may be reduced - using thrombolytic medication, though this treatment has its share of possible secondary hemorrhagic complications. Early evaluation of the severity of stroke could therefore help assist the necessary fast therapeutic decision-making process. This challenge has fostered the research project from which NEURiNFARCT has originated.

Existing MRI-based approaches necessitated the injection of a contrast agent, something NEURiNFARCT could make become obsolete as the new technique only necessitates basic routine diffusion MR image sequences.

The diffusion data measure the mobility of water molecules in tissues, which is significantly reduced in the core of the infarct lesion and to a much lesser extent, in the ischemic penumbra region. Eye identification of these alterations of the MRI data in the region at risk of infarction is impossible. The new approach therefore proposes an image analysis approach based on a model of the ongoing infarct growth in brain tissues.

The results from the study published in Radiology demonstrate that NEURiNFARCT performs at least as well as alternative approaches using perfusion techniques in MRI or CT scanners, though these latter are conditioned to the delicate intravenous injection of a contrast agent. NEURiNFARCT has the secondary advantages in the context of acute emergency care that it is an automatic and standard procedure.