

Spatial Integration of Multimodal Brain Images in Cerebral Infarction

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Summary: Different structural as well as functional imaging techniques are becoming increasingly important in the investigation of patients suffering from an ischemic stroke. Available imaging procedures usually provide complementary data, but the images can not easily be compared due to differences in patient positioning, angulation, and slice thickness. We studied the value of spatial integration of images from different modalities in a patient with an ischemic stroke and used skin markers to integrate the obtained information. Computed tomography (CT), magnetic resonance imaging (MRI), ^{99m}Tc HMPAO-single photon emission computed tomography (SPECT) and magnetic resonance spectroscopic imaging (MRSI) were performed in a patient, presenting with a right sided hemiparesis caused by an ischemic stroke. Combination of MRI with CT demonstrated that the infarction visible on CT and MRI corresponded in size and volume. Furthermore, structural and functional images could readily be integrated, thus allowing us to obtain accurate information in this stroke patient. Different imaging modalities provide complementary information in the acute phase of cerebral infarction and multimodality matching can be of great value for improvement of our understanding of the pathophysiology and course of ischemic stroke.

Key words: Brain; Computed tomography; Magnetic resonance imaging; HMPAO Single photon emission computed tomography; Magnetic resonance spectroscopic imaging; Cerebral infarction; Markers; Image matching.

Introduction

Computed tomography (CT) is widely used for the diagnosis of stroke, especially for the differentiation between cerebral infarction and hemorrhage. Magnetic resonance imaging (MRI) has recently become more important in neurological imaging.

To gain more insight in the pathophysiology of cerebral infarction, functional imaging modalities are used increasingly. Single Photon Emission Computed Tomography (SPECT) gives information on cerebral blood flow, and proton MR spectroscopy (MRS) provides information on proton-containing metabolites. Recently, MR spectroscopic imaging (MRSI) has become feasible, enabling the comparison of metabolism within the core of the infarction, in the surrounding region, and in the contralateral hemisphere in one examination.

Structural and functional imaging modalities usually provide complementary information. Integration of the information obtained with different techniques is difficult, because of differences in patient positioning, angulation, and slice thickness. Methods to combine multimodal brain images are surveyed by Viergever and coworkers. This paper presents integration of information obtained from CT, MRI, SPECT, and MRSI in a patient suffering from an ischemic stroke, using a skin marker based method.

Patient and Methods

A 56-year old man was admitted to the Department of Neurology of the University Hospital Utrecht. Early in the morning he had experienced a transient asymmetry of his face and difficulty in word-finding and naming, but in the afternoon a permanent motor deficit on his right side developed. On admission clinical assessment showed right sided hemiparesis, central facial paresis, dysarthria and mild dysphasia, with communication only slightly impaired. After informed consent was given by the patient, ancillary investigations were performed according to a previously set up protocol, which was approved by the Committee on Human Investigations of the hospital. There were no contraindications to entering a strong magnetic field, or to undergo SPECT.

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The CT, MRI, SPECT and MRSI investigations all took place within one week after admission. During his clinical period, the patient recovered with only a minimal hemiparesis left. Ultrasound and angiographic examination of the extracranial portion of the internal carotid artery were performed, which showed a high grade stenosis on the left side. Carotid endarterectomy was performed. The patient was released in good clinical condition.

Non-contrast CT scan was performed on a Philips Tomoscan LX, slice thickness 5 mm and a 5 mm gap supratentorially, and 3 mm thickness with a 3 mm gap in the posterior fossa. The pixel size was approximately 0.7 mm.

MRI and proton MRSI were performed on a whole-body Philips Gyroscan 1.5 Tesla, using a standard proton head coil operating at 64 MHz. First a sagittal scout scan was performed, followed by a T2-weighted (TR=2000ms, TE=50/100ms) transversal multislice scan (14 slices, slice thickness 7 mm, interslice gap 0.7 mm). On the transversal slices the infarcted area was defined, and a rectangular region of interest (120 × 90 mm, slice thickness 25 mm) was chosen to include the infarction, but remaining within the skull to exclude lipid signals from the bone marrow and the subcutaneous fat. Automatic shimming was performed before acquisition; a line width of 7 Hz was achieved. Water suppression was based upon selective inversion and zero-crossing; phase-encoding was done in 32 × 32 steps over a field of view of 275 × 275 mm, resulting in a voxel size of 1.8 cm³, within a scan time of 35 minutes.

With MRSI we assessed the distribution of N-acetyl-aspartate (NAA, a marker of neurons), choline (Cho, a marker of membrane metabolism), creatine (Cr, often used as a reference compound) and lactate (Lac, a marker of anaerobic metabolism) within the region of interest.

Regional cerebral blood flow was assessed after intravenous administration of 800 MBq technetium-99m hexamethyl propylene amino oxime (^{99m}Tc-HMPAO); the somatic dose equivalent amounted to 13.8 mSv. A special head fixation set was used, that had recently been developed at the department of Nuclear Medicine. Acquisition was performed with a Picker PRISM[®] three detector gamma camera, using a long-bore ultra high resolution low energy fan beam collimator. Full angle acquisition was realized in step-and-shoot mode, 3 × 20 steps, 40 sec/view, in a 64 × 64 matrix, zoom × 1. Processing of the data was done after: decay correction and normalization of all views; prefiltering with a Butterworth 5.40 filter; filtered backprojection (Metz filter); slice reconstruction, 1 pixel/slice, both transversal (which was used for matching) and parallel to the skull base ('oblique transaxial') as well as perpendicular to the skull base ('oblique coronal'). In plane resolution was 7.5 mm

FWHM. Slice thickness was approximately 7 mm.

To integrate the information obtained from the different imaging techniques, skin markers were used (Van den Elsen et al. 1991a), which were positioned at the nasion and preauricular points, after marking of the skin with long lasting dye.

The reference points indicated by the markers are used to calculate the three-dimensional transformation that relates two images, after which one of the images can be 'resliced' with slice spacing, scaling, and orientation matching those of the other image (Van den Elsen and Viergever 1991b). Corresponding slices can then be easily compared. For both MRI and CT investigation, triangular markers are used carrying contrast agent containing tubes to indicate reference points with subslice accuracy. For SPECT the marker consists of a small circular piece of filtering paper, soaked with one droplet of a ^{99m}Tc-HMPAO solution (specific activity 20 MBq/ml). MRI and MRSI have the same angulation. The slice thickness and pixel size of MRSI however, are larger than of MRI.

Results

CT on admission showed no abnormalities, especially no evidence of hemorrhage. On a second CT (performed 4 days after admission) as well as on MRI (6 days after admission) a left basal ganglia infarction was observed.

On SPECT (performed 2 days after admission) perfusion deficits were predominantly observed in the left hemisphere: inferior and mesio-temporal, in the basal ganglia, subcortical just above the level of the basal ganglia and inferior frontal. In the right hemisphere cortical and subcortical perfusion deficits were observed inferior frontal.

On MRSI (performed at the same time as the MRI, that is 6 days after admission) a decrease of NAA was observed in the hyperintense area on MRI. Lac was, although in a small amount, observed in a larger area than the NAA decrease (also near the hyperintense area on MRI). The Cr metabolite map showed a symmetrical, normal pattern over the total region of interest. A decrease of Cho was observed near the hyperintense area on MRI, but not totally overlapping with the NAA decrease or Lac increase.

After integration of the CT scan and the MRI, we found that the area of infarction corresponded very well in site, size and volume on both images (figures 1a and 1b).

After integrating the SPECT, MRI and MRSI images, we found that the perfusion deficit observed on SPECT corresponded partly with the hyperintense area observed on MRI. The hyperintense area on MRI, however, was larger in the AP direction but somewhat narrower in the left-right direction than the perfusion deficit on

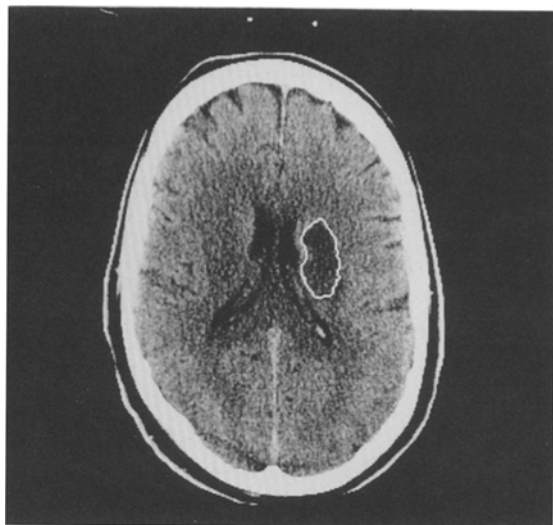


Figure 1a. CT scan performed 4 days after admission. The infarction is visible as a hypodense area. The contour of the infarction on the matched MRI is overlaid on the original CT scan.

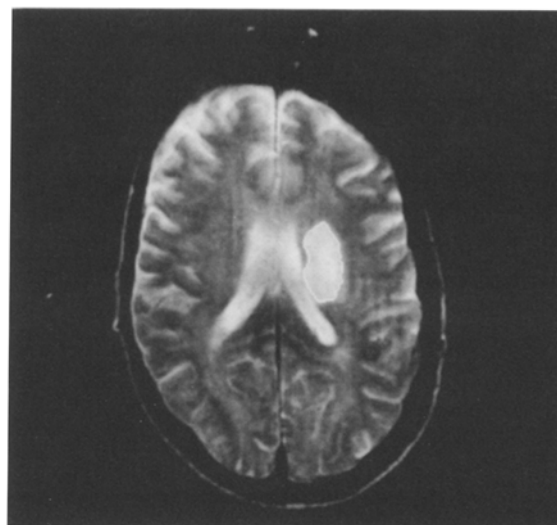


Figure 1b. MRI performed 6 days after admission, matched and resliced to correspond with the CT scan. The infarction is visible as a hyperintense area, and is contoured.

SPECT (figure 3a).

The decrease of NAA was observed in the center of the hyperintense area visible on MRI (figure 3d) as well as in the center of the perfusion deficit on SPECT (figure 3b). The area of decreased Cho was found more medially than the decrease of NAA, and both in and medial to the hyperintense area on MRI and the perfusion deficit on SPECT. A small amount of lactate was observed both in and just lateral to the hyperintensity visible on MRI (figure 2) and the perfusion deficit visible on SPECT (figure 3c); this area of increased lactate was larger than the area of NAA decrease.

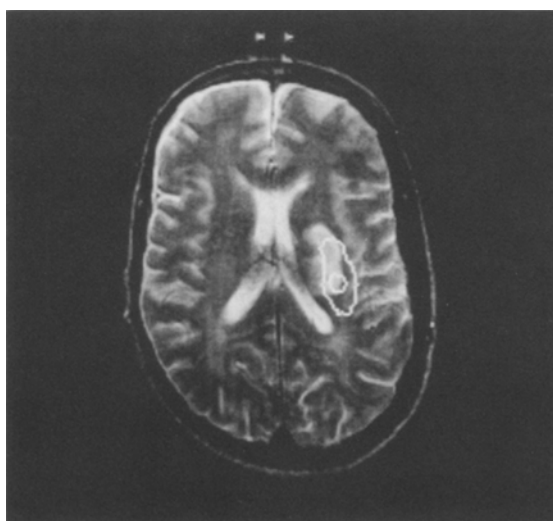


Figure 2. Original MRI. The contour of the high lactate area on MRS is overlaid on the MRI.

Discussion

Although at present it is possible to obtain structural as well as functional information in patients suffering from ischemic stroke, comparison of data acquired from different modalities appears to be difficult. Skin markers have been proven useful for the spatial integration of information obtained from different modalities.

Most cerebral infarctions are not visible on CT within the first 24 hours after the onset of symptoms. However, hemorrhages are clearly visible, which is of particular importance in the decision of interventional therapy. In contrast to CT, which is dependent on tissue attenuation of X-rays, the MR image derives its contrast from three tissue specific variables: proton density, and the T1 and T2 relaxation times. The infarcted area can be detected within 1 or 2 hours after the infarction (van Rijen et al. 1988; and Yuh et al. 1991). Compared to CT, MRI is superior in detecting small infarcted areas and in imaging the posterior fossa and the temporal lobes. MRI can visualize an infarcted area earlier than CT. Furthermore, after 2 or 3 weeks the infarcted area may appear isodense on CT scan, and therefore may be invisible. This so-called 'fogging effect' is absent on MR images (Ramadan et al. 1989).

For cerebral blood flow (CBF) imaging, SPECT is now a widely available nuclear imaging technique. ^{99m}Tc-HMPAO crosses the blood brain barrier following intravenous injection, and distributes within the brain in proportion to the regional CBF, where it remains fixed long enough to be imaged. In the acute phase of cerebral infarction, SPECT will show an area of non-perfusion.

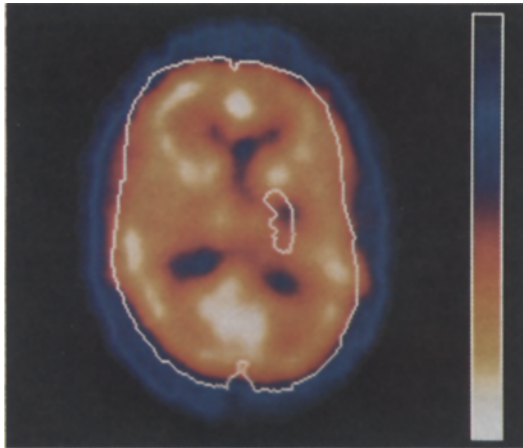


Figure 3a. SPECT, matched and resliced to correspond with the MRI. The contours of the MRI brain and infarction are overlaid on the SPECT.

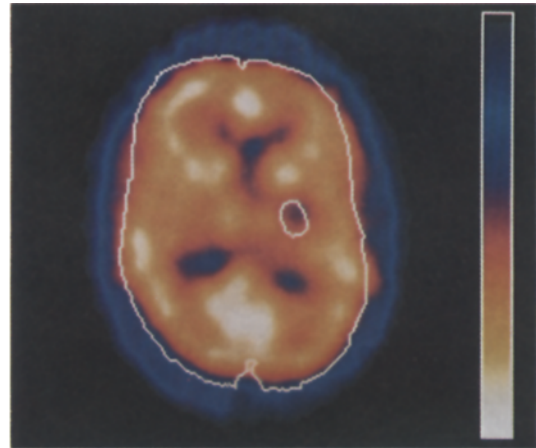


Figure 3b. SPECT, matched and resliced to correspond with the MRI. The contours of the brain obtained from MRI and of the area with NAA decrease on MRS are overlaid on the SPECT.

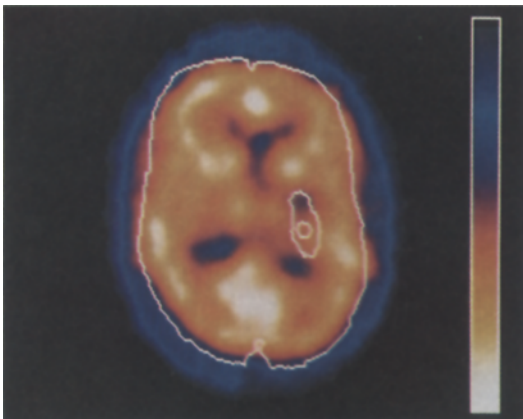


Figure 3c. SPECT, matched and resliced to correspond with the MRI. The contours of the brain obtained from MRI and of the high lactate area on MRS are overlaid on the SPECT.

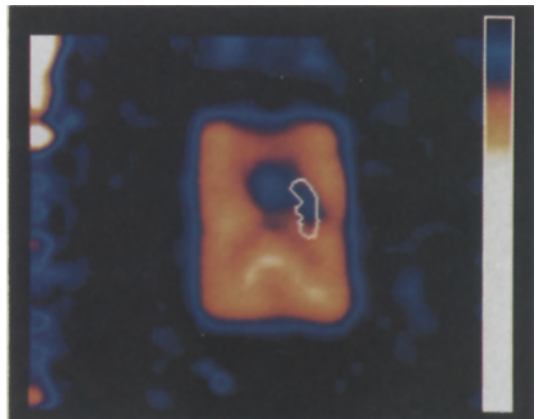


Figure 3d. NAA metabolite map. The contour of the infarction on MRI is overlaid on the NAA map.

With proton MR spectroscopy, NAA, a compound only found in neurons (Birken and Oldendorf 1989), Cr, frequently used as a reference compound, Cho, a marker of membrane metabolism, and Lac, a marker of anaerobic metabolism, can be detected. In cerebral infarctions a decrease in NAA and an increase in Lac can be observed. The Cho content can either be constant, or, sometimes be decreased.

A striking point in our results is the fact that the observed infarcted area on CT and MRI overlapped completely. From the literature it is well known that with MRI not only infarction but also edema formation is

observed, and that these areas can not readily be distinguished. In this case the area of infarction on CT and MRI corresponded in size and position. This suggests that on CT to some extent edema overlaps with the observed hypodense area.

NAA is a neuronal marker, and a decrease is found if neurons have died (Peres et al. 1992); therefore, we conclude that the area with low NAA, in the center of the lesions on MRI and SPECT, is the area of infarction. Our Cr metabolite map showed a symmetrical pattern without a decrease of Cr in or around the hyperintense area seen on MRI. Although Fenstermacher and Narayana (1990) found a decrease of Cr in the infarcted area, other authors (Kobayashi et al. 1977; Nordstrom et

al. 1978 and Petroff et al. 1988) did not find alterations in Cr in ischemic conditions, which is in agreement with our findings. The decrease of Cho was observed predominantly medial to the area with NAA decrease (i.e., the infarcted area), and obviously was not caused by cavity formation. Also, there was no overlap between the area with high Lac and the area with Cho decrease. Therefore, there was no indication that in the low Cho area ongoing ischemia was present. It is well known that in case of an ischemic infarction edema formation occurs, and it is possible that a decrease of Cho spectral intensity can be attributed to a diluting effect on the choline concentration, as has been described before (Bruhn et al. 1989). The fact that the low Cho area was observed partially in the lesion on MRI, but not overlapping with the other metabolite abnormalities, points in the same direction. The position of the area with low Cho with respect to the hyperintense area on MRI, could be an indication that not all edema accompanying ischemic stroke is visible with MRI. The fact that Lac was not only found in the hyperintense area seen on MR image, but exceeded laterally, has been described before (Berkelbach van der Sprenkel et al. 1988), and can indicate the existence of a penumbra. This is an area with lower perfusion, but still viable cells; when perfusion stays low or drops, cell necrosis will inevitably occur (and thus the area of infarction can become larger). When blood flow is restored in time, normal function and metabolism can recover. The amount of Lac was extremely low, which indicated that the perfusion decrease must be marginal, and may therefore be below detection with SPECT. This may be the explanation for the fact that the Lac area exceeded the perfusion deficit visible on SPECT. The low Lac level and its relation to the perfusion deficit on SPECT may be an indication for a favorable prognosis.

Conclusion

Recently developed imaging techniques provide complementary information in the acute phase of cerebral infarction, and multimodality matching can be of considerable value for improvement of our understanding of the pathophysiology of ischemic stroke.

Our results are so far based upon the investigations in one patient. Further studies are needed to establish the exact role of multimodal brain imaging in ischemic stroke.

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