

# BRAIN PERFUSION SPECT WITH 99M-TC HMPAO IN SPONTANEOUS INTRACEREBRAL HEMORRHAGE

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## ABSTRACT

Spontaneous intracerebral hemorrhage has a poor prognosis and is considered the deadliest form of stroke. Many recent studies have shown that there are many mechanisms involved in the pathology of this disease among which one of the most studied and controversial is perilesional ischemia. The aim of our study was to assess the role of brain perfusion SPECT with 99m-Tc HMPAO in demonstrating perfusion changes in brain tissue surrounding hematoma.

## 1. INTRODUCTION

Spontaneous intracerebral hemorrhage has a poor prognosis and is considered the deadliest form of stroke. It occurs in approximately 10-15% of all stroke (1, 2) and has a higher incidence in populations with a high incidence of untreated essential hypertension.

Many recent studies have shown that there are many mechanisms involved in the pathology of this disease: edema formation and extension, ischemia, inflammation, thrombin activation, rebleeding, reperfusion, metabolic changes, apoptosis...

All of these factors (and maybe many others) are affecting brain tissue surrounding hematoma and are responsible of the progressive neurological deterioration and of the poor prognosis.

Most of these damages are not revealed by anatomical imaging techniques (CT or MRI).

## 2. PURPOSE

The aim of our study was to assess the role of brain perfusion SPECT with HMPAO in demonstrating perfusion changes in brain tissue surrounding hematoma.

## 3. METHOD

We performed brain perfusion SPECT in 17 pts with primary intracerebral hemorrhage, within an interval of 24h to 4 days from the onset of stroke. Acquisition has been made 30 min after iv inj of 25 mCi of 99mTcHMPAO, by using a dual head gamma

camera Philips Axis. In all patients we visually compared the images with the CT scan, performed in the same day with brain SPECT. We assessed and reported our results after analyzing the diameter of perfusion defect on both scans and by means of the presence/absence of perfusion changes in the cerebral tissue adjacent to the hematoma and at distanced areas.

## 4. RESULTS

In 14 patients (82.35%) perfusion defect corresponding to hematoma was greater than expected after CT scan. In 2 patients hematoma maximum diameter was comparable on CT and on SPECT images; in 1 patient with intraventricular hemorrhage we found a quasinormal aspect of the perfusion study (figure 1).

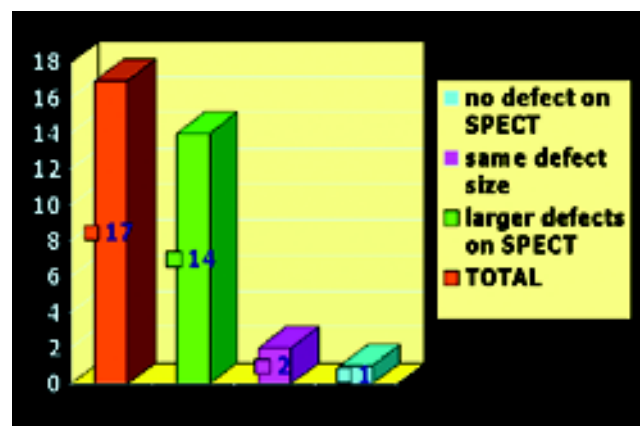
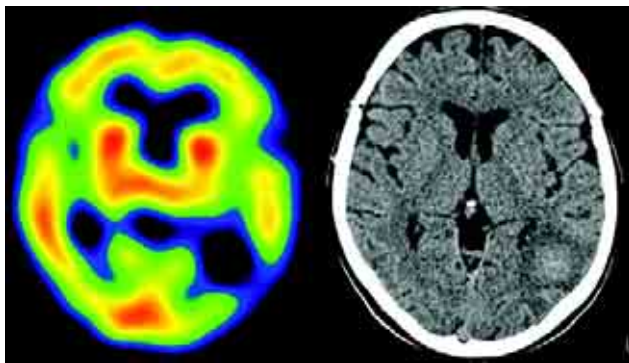


Figure 1

Most of our patients (82.35%) shown a larger defect size on SPECT than expected after CT

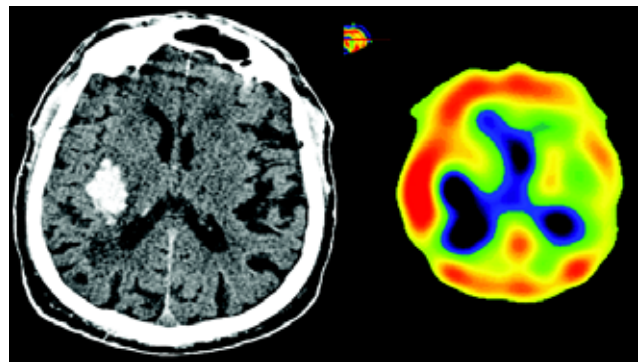


**Figure 2**

*Hematoma surrounded by a large hypoperfused area*

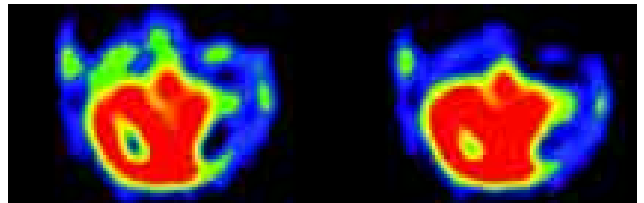
In the group of patients with larger perfusion defect, SPECT revealed a large cold spot with a similar size compared with CT and a surrounding hypoperfused area (figure 2).

In 6 patients imaged at 36-72 h from onset, SPECT revealed an area of hyperperfusion in the peripheral cortex, adjacent to hypoperfused area and corresponding to a normal-appearing brain tissue on the CT scan (figure 3). In 2 patients we found cortical hypoperfused area in the contralateral cortex, with normal appearing brain tissue on



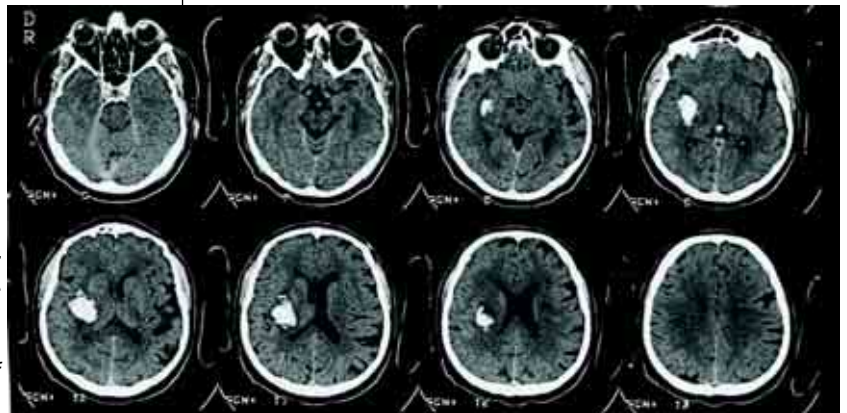
**Figure 3**

*CT scan (left) and brain perfusion SPECT (right). We can notice, on the SPECT scan, the cold spot corresponding to hematoma on CT, with a small hyperperfused area in the peripheral cortex, with a normal aspect on CT (luxury perfusion?)*



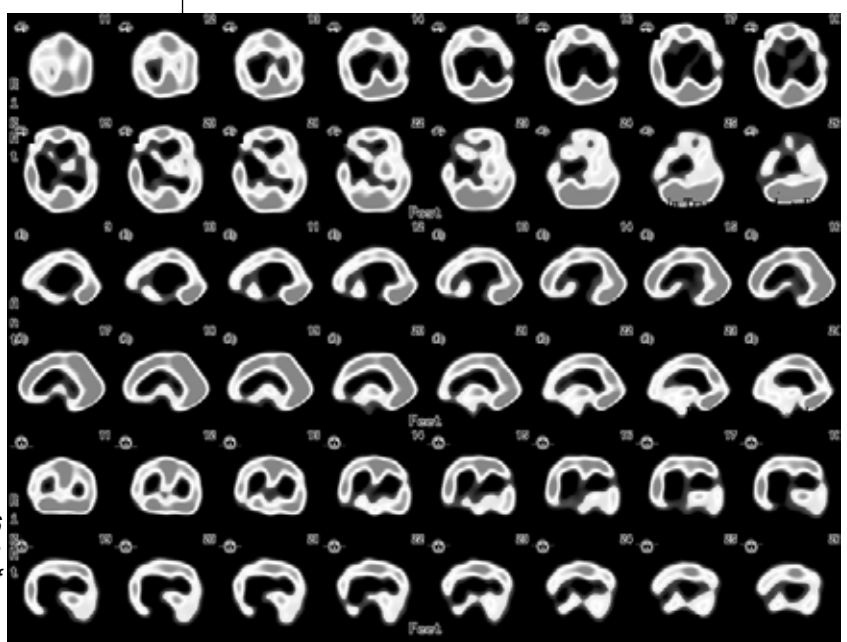
**Figure 4**

*Cerebellar Diaskisis. 57 years old male with left putaminal hemorrhage. SPECT study revealed a right cerebellar cold spot in a patient with left thalamic hematoma*



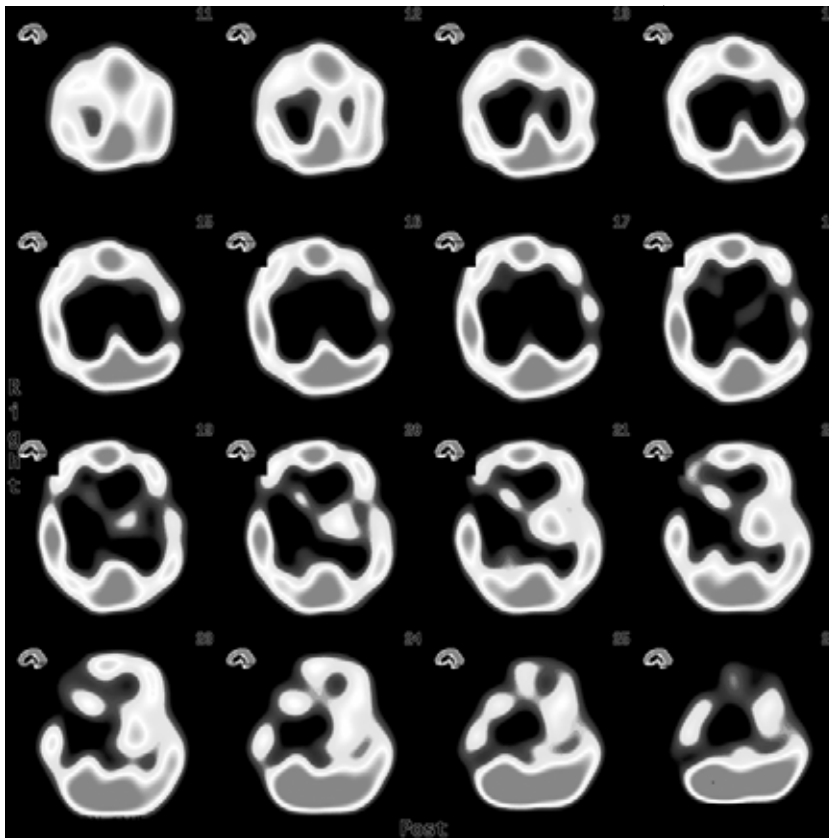
**Figure 5**

*CT scan reveal an area with hematic density in the right putamen, external capsule and corona radiata. We can also notice a small surrounding area of perilesional oedema.*

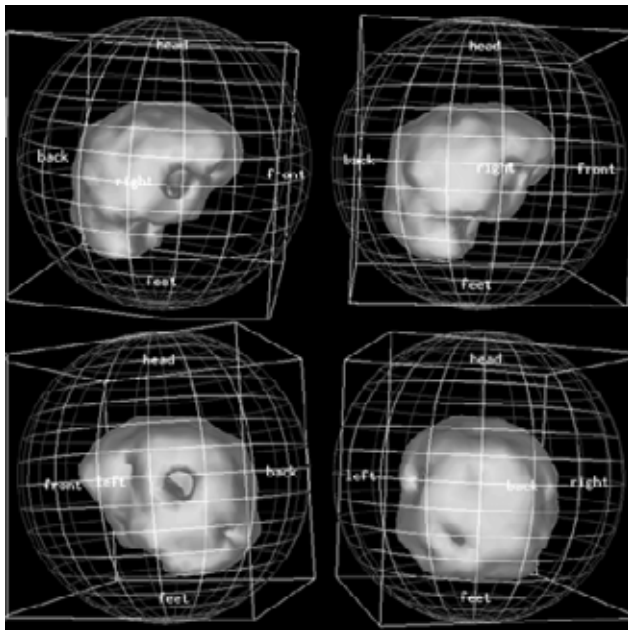


**Figure 6**

*Cold spot in right thalamus, corresponding to the hematoma. Reduced uptake of radiotracer in the basal nucleus, dorsolateral cortex and temporal.*



**Figure 7**  
Reduced uptake of radiotracer (hypoperfusion) in the parieto-occipital cortex, left inferior cortex with extension to left occipital.



**Figure 8**  
3D reconstruction. We have to note the cold spots on the cortex surface.

CT. In 3 patients we found crossed cerebellar diaschisis (figure 4).

## 5. CASE REPORT

52 years old male with hemorrhagic stroke underwent same day CT and  $^{99m}\text{Tc}$ -HMPAO SPECT scan. The most relevant images will follow in the figures 5-8.

## 6. DISCUSSIONS

Despite the latest advances in medical treatment of hypertension and neurocritical care, patients suffering SICH still have a very poor prognosis, with a greater mortality and larger neurological deficits at the survivors than for ischemic stroke or for subarachnoid hemorrhage.

In recent years many effort have been made for developing experimental models in order to better asses the pathophysiology of ICH. There have been recognized a primary tissue injury due to the hematoma formation, and a secondary brain injury which occurs in time, in which it was thought to be determined by the mass effect and edema. The roles of edema, ischemia, mass effect, direct cellular toxicity, inflammation, and apoptosis are being evaluated in experimental studies of ICH.

In 1902, Cushing described the brain injury after hematoma formation – to be the result of local pressure compressing the microcirculation and causing ischemia around a hematoma (3). In 1981, Astrup et al (4) proposed the term „ischemic penumbra“ to describe brain with CBF values above a lower limit of membrane dysfunction and cell death, but below an upper limit corresponding to electrophysiological dysfunction. During the past years many experimental models and human studies demonstrated a zone of perilesional ischemia around ICH and have suggested the potential for perfusion recovery in these

areas. Most of them support the theory of a decreased CBF adjacent to the hematoma, and gave evidence of histological ischemic changes in perihematomal brain tissue. In 1994, Young et al have suggested that the primary cause of edema formation in experimental models of ICH may be local tissue ischemia. (5)

Siddique et al (6) have documented that some of the hypoperfused tissue surrounding ICH regains its perfusion in the long term (penumbra), and suggested that medical or surgical therapeutic interventions could increase the volume of perilesional brain that recovers after the initial insult and therefore supporting the idea that therapeutic intervention in ICH has the potential to reduce the ultimate neurological deficit and improve outcome.

In a serial SPECT study on 13 hypertensive ICH patients, Murakami et al correlated changes in rCBF on a long term follow up (55 weeks) – with clinical outcome. They found that increased rCBF over time may have a favorable outcome, while patients with decreased and/or unchanged rCBF over-time neurological deficits were greater (7).

Several authors have suggested that perilesional hypoperfusion occurs without ischemia as a result of reduced metabolic demand or diaschisis (8, 9). In a study of 23 patients with ICH studied using SPECT scanning, perilesional blood flow was found

to be lowest during the first 24 hours post ictus, but it normalized as edema formed over the next 2 to 3 days. (10).

In a small study in which positron emission tomography was used, no zone of tissue hypoxia or „ischemic penumbra“ was identified. (11). Another very recent PET study on metabolic changes in ICH using PET have shown a high <sup>11</sup>C-methionine uptake and decreased <sup>18</sup>F-FDG uptake (12).

It is possible that in the very near future PET will have an increasingly role in studying biochemical changes that occurs in ICH. Up to now, only studies on very small series of patients have been published.

## 7. CONCLUSION

Brain perfusion SPECT revealed not only the irreversible cerebral lesions of the brain within the cold area of the hemorrhage, but also hypoperfused areas surrounding the hematoma. These areas contain viable brain tissue that may be a target for future neuroprotective therapeutic strategies. We can conclude that brain perfusion SPECT could play an important role in evaluating patients with hemorrhagic stroke, by early demonstrating severe functional changes responsible of clinical deterioration, thus allowing prompt dedicated therapeutic intervention.

## REFERENCES

1. **Matthew E Fewel, MD, B Gregory Thompson, Jr, MD, And Julian T Hoff, MD** – Spontaneous Intracerebral Hemorrhage: a Review. *Neurosurg Focus*, 15 (4): Article 1, 2003.
2. **Dennis MS, Burn JP, Sandercock PA et al** – Long-term survival after first-ever stroke: the Oxfordshire Community Stroke Project. *Stroke*, 24:796–800, 1993.
3. **Cushing H** – Some experimental and clinical observations concerning states of increased intracranial tension. *Am J Med Sci*, 124: 375-400, 1902.
4. **Astrup J, Siesjö BK, Symon L** – Thresholds in cerebral ischemia – the ischemic penumbra. *Stroke*, 12: 723-725, 1981.
5. **Yang GY, Betz AL, Chenevert TL et al** – Experimental intracerebral hemorrhage: relationship between brain edema, blood flow, and blood-brain barrier permeability in rats. *J Neurosurg*, 81: 93-102, 1994.
6. **Siddique MS, Fernandes HM, Wooldridge TD et al** – Reversible ischemia around intracerebral hemorrhage: a single-photon emission computerized tomography study. *J Neurosurg*, 2002, Apr; 96(4):736-741.
7. **Murakami M, Fujioka S, Oyama T** – Serial changes in the regional cerebral blood flow of patients with hypertensive intracerebral hemorrhage – long-term follow-up SPECT study. *J Neurosurg Sci*, 2005 Sep; 49(3): 117-124.
8. **Schellinger PD, Fiebich JB, Hoffmann K et al** – Stroke MRI in intracerebral hemorrhage: is there a perihemorrhagic penumbra? *Stroke*, 34: 1674-1679, 2003.
9. **Zazulia AR, Diringer MN, Videen TO et al** – Hypoperfusion without ischemia surrounding acute intracerebral hemorrhage. *J Cereb Blood Flow Metab*, 21: 804-810, 2001.
10. **Mayer SA, Lignelli A, Fink ME et al** – Perilesional blood flow and edema formation in acute intracerebral hemorrhage. A SPECT study. *Stroke*, 29: 1791-1798, 1998.
11. **Hirano T, Read SJ, Abbott DF et al** – No evidence of hypoxic tissue on <sup>18</sup>F-fluoromisonidazole PET after intracerebral hemorrhage. *Neurology*, 53: 2179-2182, 1999.
12. **Kuwabara Y, Sasaki M** – <sup>11</sup>C-methionine uptake in cerebrovascular disease: a comparison with <sup>18</sup>F-FDG PET and <sup>99m</sup>Tc-HMPAO SPECT. *Ann Nucl Med*, 2002 May; 16(3): 207-211.
13. **Raymond A Swanson** – Intracerebral Hematoma: Beyond the Mass Lesion. *Stroke*, 2006; 37: 2445.
14. **Wagner KR, Sharp FR, Ardizzone TD, Lu A, Clark JF** – Heme and iron metabolism: role in cerebral hemorrhage. *J Cereb Blood Flow Metab*, 2003; 23: 629-652.
15. **Keep RF, Xi G, Hua Y, Hoff JT** – The deleterious or beneficial effects of different agents in intracerebral hemorrhage: think big, think small, or is hematoma size important? *Stroke*, 2005; 36: 1594-596.
16. **Kim-Han JS, Kopp SA, Dugan LL, Diringer MN** – Perihematomal mitochondrial dysfunction following intracerebral hemorrhage. *Stroke*, 2006; 37: 2457-2462.