SCINTIGRAPHY OF THE CENTRAL NERVOUS SYSTEM
Part 1: Introduction and BBB studies

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FIRST PART

INTRODUCTION

AND

METHODOLOGY
RADIOISOTOPES IN NUCLEAR MEDICINE

CLINICAL USE

PATIENT IMAGING

Planar and SPECT:

Positron Emittance Tomography:

PATIENT THERAPY:

IN VITRO STUDIES:
RADIOISOTOPES IN NUCLEAR MEDICINE

CLINICAL USE

PATIENT IMAGING

Planar and SPECT:  Single Photons emitters (γ, x)
                  (99mTc, 201TI)

Positron Emission Tomography:  Positron emitters (e+)
                                (18F, 82Rb)

PATIENT THERAPY:  Particular radiation emitters (e,α)
                  (131I, 90Y)

IN VITRO STUDIES:  Low energy emitters (γ,e)
                  (125I, 3H, 14C)
SCINTIGRAPHY OF THE CENTRAL NERVOUS SYSTEM

- DYNAMIC FIRST PASS FLOW STUDY
- CISTERNOGRAPHY
- SHUNTOGRAM
- TUMOR IMAGING
- FUNCTIONAL SPECT/PET OF THE BRAIN
SCINTIGRAPHY
OF THE CENTRAL NERVOUS SYSTEM

- **DYNAMIC FIRST PASS FLOW STUDY**
  - Diagnosis of Cerebral Death
- **CISTERNOGRAPHY**
  - Normal Pressure Hydrocephalus, CSF leaks
- **SHUNTOGRAM**
  - Patency/Function of shunts
- **TUMOR IMAGING**
- **FUNCTIONAL SPECT/PET OF THE BRAIN**
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- **DYNAMIC FIRST PASS FLOW STUDY**
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- **CISTERNOGRAPHY**
  - Normal Pressure Hydrocephalus, CSF leaks

- **SHUNTOGRAM**
  - Patency/Function of shunts

- **TUMOR IMAGING**
  - Grading, Differentiation, Recurrence

- **FUNCTIONAL SPECT/PET OF THE BRAIN**
  - Regional Cerebral Blood Flow
  - Regional Cerebral Metabolism (Glucose/AA/F-DOPA)
  - Regional Cerebral Receptor Studies
BASIC BIOLOGIC CONCEPTS FOR BRAIN IMAGING

THE BLOOD-BRAIN BARRIER (BBB)

a) Imaging Agents, which do not cross the normal BBB
(normal brain appears non-active)
but they cross the broken BBB
and show lesions as hot spots

b) Imaging Agents, which cross the normal BBB
(normal brain appears active)
and show some lesions as cold spots
and some as hot spots
A. Radiopharmaceuticals Labeled with Single Photon Emission Radionuclides

a) With agents which DO NOT CROSS THE NORMAL BBB and DO NOT ACCUMULATE IN THE NORMAL BRAIN
   \(^{99m}\text{Tc-PTC, DTPA, GH and MAG}_3\) Brain Studies, \(^{201}\text{TI}\)

b) With agents which CROSS THE NORMAL BBB and ACCUMULATE WITHIN THE NORMAL BRAIN
   \(^{99m}\text{Tc-HMPAO, }^{99m}\text{Tc-ECD, }^{123}\text{I-IBZM, }^{123}\text{I-IQN}\)

c) With agents for INTRATHecal INJECTION
   \(^{111}\text{In -DTPA}\)
## B. Radiopharmaceuticals Labeled with Positron Emission Radionuclides

They all cross the normal BBB

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{11}$C(20min)-Carbon Monoxide</td>
<td>Blood Pool-Volume</td>
</tr>
<tr>
<td>$^{11}$C-Carbon Dioxide</td>
<td>Tissue pH</td>
</tr>
<tr>
<td>$^{11}$C-Dopamine</td>
<td>Neuroreceptors</td>
</tr>
<tr>
<td>$^{11}$C-N-methyl-spiperone</td>
<td>Neuroreceptors</td>
</tr>
<tr>
<td>$^{13}$N(10min)-Ammonia</td>
<td>Perfusion</td>
</tr>
<tr>
<td>$^{13}$N(10)-Amino Acids</td>
<td>Tumors</td>
</tr>
<tr>
<td>$^{15}$O$_2$(2min) - Oxygen</td>
<td>Metabolism/Tumors</td>
</tr>
<tr>
<td>$^{15}$O$_2$(2min) - Water</td>
<td>Blood Flow</td>
</tr>
<tr>
<td>$^{18}$F(110min)-2 Deoxy-D-glucose</td>
<td>Metabolism/Tumors</td>
</tr>
<tr>
<td>$^{18}$F-Haloperidol</td>
<td>Neuroreceptors</td>
</tr>
<tr>
<td>$^{18}$F-DOPA</td>
<td>Basal Ganglia / Tumors</td>
</tr>
</tbody>
</table>
POSITRON EMISSION TOMOGRAPHY (PET)  
(COINCIDENCE DETECTION PRINCIPLE)  
(TIME OF FLIGHT PRINCIPLE)

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Half-Life (min)</th>
<th>Positron Yield</th>
<th>Positron Energy (MeV)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Future plans:</strong> Cyclotron-Produced</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$^{15}$O</td>
<td>2.04</td>
<td>99+%</td>
<td>1.72</td>
</tr>
<tr>
<td>$^{13}$N</td>
<td>9.96</td>
<td>99+%</td>
<td>1.19</td>
</tr>
<tr>
<td>$^{11}$C</td>
<td>20.4</td>
<td>99+%</td>
<td>0.96</td>
</tr>
<tr>
<td><strong>Currently used:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$^{18}$F</td>
<td>110.0</td>
<td>96.9%</td>
<td>0.64</td>
</tr>
<tr>
<td><strong>Generator-Produced</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Near Future plans:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$^{82}$Rb</td>
<td>1.26</td>
<td>96%</td>
<td>3.35</td>
</tr>
<tr>
<td>$^{68}$Ga</td>
<td>68.1</td>
<td>90%</td>
<td>1.90</td>
</tr>
</tbody>
</table>
PROPERTIES OF POSITRON EMITTERS

• CHEMICAL
  Can Label Metabolic Molecules (Glucose, AA, etc)

• PHYSICAL
  ✓ Small: **Do not alter the Biochemical Properties**
    of the Metabolic Molecules (**Biochemical Recognition Maintained**) Therefore allow **Molecular Imaging**

  ✓ Emit Positrons: **Need special Cameras** (PET cameras)
    Allow **Tomography and Quantitation**

  ✓ Have short half lives: **Low Radiation Exposure**

  ✓ **Need Cyclotrons** to produce them (or special generators)
EXAMPLES OF BRAIN SCINTIGRAPHY
NORMAL BRAIN FLOW STUDY with agents which do not cross the Normal BBB (with $^{99m}$Tc-PTc, DTPA, GH, MAG$_3$)

- Anterior cerebral arteries
- Middle cerebral artery
- Carotid artery

Arterial phase
Capillary phase
Venous phase
Superior sagittal sinus

First Pass Flow Study
Static Images
Normal Study with agents which do not cross the Normal BBB
(Thallium-201). The Normal brain is not visualized. The skull is

Normal Study with agents which cross the Normal BBB
(HMPAO, ECD, FDG). The Normal brain (cortex) is visualized.
NORMAL BRAIN FLOW STUDY with agents which cross the Normal BBB (with $^{99m}$Tc-HMPAO, $^{99m}$Tc-ECD)
1. Timely filling and emptying of the cisternae and the subarachnoid space
2. No filling of the ventricles (= no reversal of the CSF flow.)
NORMAL CISTERNOGRAPHY SPECT
Three Plane Tomograms

Volume Reprojection Frames
FDG / PET NORMAL AND IN ALZHEIMER’S DISEASE

NORMAL

ALZHEIMER’S
PET FDG IN BRAIN TUMORS

MRI cannot differentiate between recurrence and necrosis.

FDG/PET shows recurrence (arrows) amidst necrotic (non-radioactive) area.
SEROTONIN RECEPTORS

Normal Brain Study

After 3mo on Ecstasy
SECOND PART

CLINICAL APPLICATIONS
SCINTIGRAPHY OF THE BRAIN

A. WITH RADIOPHARMACEUTICALS WHICH DO NOT CROSS

THE NORMAL BLOOD-BRAIN-BARRIER
DIAGNOSIS OF CEREBRAL DEATH

DYNAMIC FIRST PASS FLOW STUDY

$^{99m}$Tc-PTc, DTPA, GH, $^{3}$MAG First Pass Flow

($^{99m}$Tc- HMPAO or ECD)
BRAIN DEATH: DEFINITION

Brain Death results from total cessation of cerebral blood flow and global infarction of the brain at a time when respiration is preserved with artificial support and the heart continues to function.

It is the only irrevocable loss of brain function currently recognized by law as death.

Brain Death is a clinical diagnosis! Laboratory tests serve as confirmatory signs.

Brain Death is a Critical diagnosis whenever organ donation for transplantation is considered and the donor has to be transferred to the operating room while cardiac and respiratory function persists.
BRAIN DEATH: CONFIRMATORY TESTS

- Isoelectric Electro Encephalo Gram (Must exclude profound hypothermic, hypotensive, or drug-induced CNS depression)
- Doppler measurements of brain flow
- Four vessel Cerebral Angiogram
- CT imaging after inhalation of stable xenon
- MRA
- First Pass Radionuclide Cerebral Blood Flow Study
BRAIN (CEREBRAL) DEATH

Cessation of Cerebral Blood Flow is a Confirmatory Sign of Brain Death

First-Pass Radionuclide Flow study:

Portable $\gamma$-Camera, $^{99m}$Tc-MAG$_3$, (or other BBB) 5min study

Non-visualization of arterial, capillary and SSS activity during the first pass is a confirmatory sign of Cerebral Death

This is the last sign to develop in the process of Brain Death
BRAIN DEATH ASSESSMENT BY SCINTIGRAPHY
First Pass Radionuclide Cerebral Blood Flow Study

- Reliable, safe, and cost-effective bedside
- Adults and children
- The last objective finding to develop
- It is not due to an increase in intracranial pressure and it is not associated necessarily with thrombosis of the vessels
FIRST PASS RADIONUCLIDE CEREBRAL BLOOD FLOW STUDY: Technical Issues

- Adequate Dose (5-30mCi MAG₃) or HMPAO or ECD
- Good bolus
- Must see flow to both common carotids
- Some use an elastic band around the head just above the orbits.
- It is our experience that MAG₃ is the agent of choice, not ECD etc.
A study is presented to you for evaluation for cerebral death
FIRST PASS RADIONUCLIDE CEREBRAL BLOOD FLOW STUDY

Tc-GLUCOHEPTONATE DOES NOT CROSS BBB

There is evidence of Cerebral Blood Flow
A study is presented to you for evaluation for cerebral death
FIRST PASS RADIONUCLIDE CEREBRAL BLOOD FLOW STUDY
MAG₃, DOES NOT CROSS THE BBB

There is evidence of Cerebral Blood Flow
A study is presented to you for evaluation for cerebral death
There is evidence of Cerebral Blood Flow

Activity fixed in the cortex
In the presence of activity in the carotid arteries, a Lack of Cerebral Perfusion is a Positive Result and this is diagnostic of Cerebral Death.

- It is the Last test to become Positive.
- It is Irreversible and equivalent to Cerebral Death.
- However, in the presence of Cerebral Death, Brain Stem and Cerebellum may still be alive.
- The test must be of excellent quality.
A study is presented to you for evaluation for cerebral death
Patient with no flow but late visualization of the SSS

Lack of Cerebral Perfusion

No arterial flow

No visualization of the SSS
A study is presented to you for evaluation for cerebral death
FIRST PASS RADIONUCLIDE CEREBRAL BLOOD FLOW STUDY
MAG3, DOES NOT CROSS THE BBB
Lack of Cerebral Perfusion

No arterial flow
No visualization of the SSS

Is this the SSS?
No, Superficial Vein
A study is presented to you for evaluation for cerebral death
FIRST PASS RADIONUCLIDE CEREBRAL BLOOD FLOW STUDY
GH, DOES NOT CROSS THE BBB

There is evidence of Cerebral Blood Flow

Patient sp stroke: Right Middle Cerebral Artery Infarct
A study is presented to you for evaluation for cerebral death
First Pass Flow Study

There is evidence of Cerebral Blood Flow in the right hemisphere

Tomographic (SPECT) Flow Study

Static Planar Study
NORMAL PRESSURE HYDROCEPHALUS

LEAKS OF CEREBROSPINAL FLUID

CISTERNOGRAPHY
CISTERNOGRAPHY

METHOD

Intrathecal injection (L₄-L₅) 0.5-1.0mCi $^{111}$In-DTPA, which normally does not cross the ependyma and does not enter the ventricular system.

Imaging at 24-48 - 72 hrs to study CSF kinetics and search for ventricular filling or other abnormalities.

INDICATIONS

Diagnosis of Normal (Low) Pressure Hydrocephalus and Cerebrospinal Fluid Leaks.
A patient with mental and walking problems and urine leaks
CT: Hydrocephalus
CSF pressure was found normal
Evaluate for NPH
CISTERNOGRAPHY: Principle and Methodology

**111In-DTPA does not cross the ependyma**
It is removed from the Subarachnoid Space by the arachnoid granulation (pacchionian bodies) which normally drain the Cerebrospinal Fluid into the Superior Sagittal Sinus (SSS)
It does not enter the ventricular system

**Imaging Technique:**
Combination of Planar and SPECT imaging
Planar images at 24 - 48 - 72 hrs, and a SPECT at 24 hrs to confirm or exclude ventricular filling and localize leaks

**Normal CSF Kinetics:**
After an Intrathecal Injection of 0.5-1 mCi **111In-DTPA**
at 4 hr, the activity is in the basal cisternae (cerebellopontine)
at 24hr activity is in the silvian cisternae and around the brain
at 48hr it is mostly around the convexities and the SSS and
at 72hr it remains only around the convexities and the SSS
1. Timely filling and emptying of the cisternae and the subarachnoid space

2. No filling of the ventricles (?) (= no reversal of the CSF flow?)
NORMAL (!) CISTERNOGRAPHY PLANAR and SPECT

Timely filling and emptying of the cisternae and the subarachnoid space
(from the planar study)

Three Plane Tomograms

No filling of the ventricles! (= no reversal of the CSF flow! )
A patient with mental and walking problems and urine leaks
CSF pressure was found low
CT: Hydrocephalus
Evaluate for NPH
NORMAL PRESSURE HYDROCEPHALUS

Pathophysiology

Adhesions in the Subarachnoid Space around the convexities lead to temporary impairment of drainage of CSF and increased pressure, which causes Reversal of Flow into the Ventracles and Hydrocephalus with eventual compensation of the system (pressure becomes normal).

Characteristics

- Preservation of a Normal CSF Pressure
- Slow Kinetics of the CSF and
- Ventricular Filling after intrathecal injection of $^{111}$In-DTPA
CISTERNOGRAPHY-PLANAR
NORMAL PRESSURE HYDROCEPHALUS

Ventricular filling, Slow clearance: NPH
CISTERNOGRAPHY-SPECT
NORMAL PRESSURE HYDROCEPHALUS

Marked Hydrocephalus, Confirmation of Ventricular Filling
A 7 yo boy had a history of repeated meningitis

Cerebrospinal Fluid Leak was suspected
CEREBROSPINAL FLUID RHINORHEA

24 hr Lateral View of Cisternogram

CSF Rhinorhea
A 44 yo male following a benign tumor removal from the thoracic spine developed headaches and walking problems. CSF pressure was found low.
CSF Leak from the upper thoracic spine

<table>
<thead>
<tr>
<th>Time</th>
<th>Ant</th>
<th>30min</th>
<th>Lat</th>
<th>4hr</th>
<th>24hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSF Leak</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
<td><img src="image5.png" alt="Image" /></td>
</tr>
</tbody>
</table>

CISTERNOGRAPHY FOR CSF LEAK
PATENCY OF SHUNTS

SHUNTOGRAM
A patient with a ventriculo-peritoneal shunt was sent to be evaluated for patency.
Dynamic studies performed after injection of $^{99m}$Tc-DTPA into the reservoir of a ventriculo-peritoneal shunt

Follow the rate of emptying

Laboratories have to develop standards and data base for normalcy
NORMAL SHUNTOGRAM

Reservoir of a ventriculoperitoneal shunt

shuntogram draining $T^{1/2}=12\text{min}$
SHUNTOGRAM: OBSTRUCTION

shuntogram showed no draining
BRAIN TUMORS

THALLIUM, GALLIUM, OCTREOSCANN
A patient with a treated malignant meningioma had a questionable MRI study and was sent for evaluation with Thallium-201
SPECT Th-201 TUMOR IMAGING: Recurrence

DD Necrosis v/s Tumor recurrence. Can Th-201 SPECT help?

Th-201 SPECT c/w Recurrence
CLINICAL APPLICATIONS OF BRAIN TUMOR SCINTIGRAPHY

- PREOPERATIVE TISSUE CHARACTERIZATION
- DIFFERENTIATION OF TUMORS FROM INFECTIONS
- THERAPY PLANNING
- EVALUATION OF EFFECTIVENESS OF TREATMENT
- DIAGNOSIS OF RECURRENCE
- PROGNOSIS BEFORE AND AFTER THERAPY
SPECT I-Methyl Tyrosine: Prognostic Information

$^{123}$I-methyl-tyrosine Tumor Scans (Post Operatively)

Patient A survived 6 months

Patient B survived 38 months

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