MDS
Science advancing health

Production and Use of Medical Isotopes from MDS Nordion

Vancouver Operations

30-Jan-06

MDS Nordion Vancouver Operations

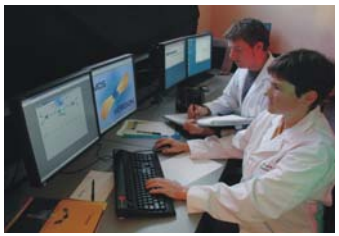
What we do at MDS Nordion

Use radioisotopes, radiation and related technologies to prevent, diagnose and treat disease.

What we <u>really</u> do...

We’re fighting disease in many countries.

Every single day, our products help people.






We're MDS Nordion, Vancouver Operations

- MDS Nordion is a Canadian life sciences company
- In Vancouver, we're located on the UBC campus where 85 people are dedicated to isotope production
- We've been in business in Vancouver over 25 years

What is a radioisotope?

- Isotope: a stable element consisting of atoms
- Radioisotope: a radioactive form of such isotopes. Being radioactive, it has the same number of protons but a different number of neutrons. This changes the characteristics of that element's nuclear behaviour, but not chemical or biological behaviour.
- As the radioactive isotope decays, it gives off energy. We harness this energy so it can be used to image the body or treat cancer

How are radioisotopes produced?

- In Vancouver, we use cyclotrons, or “giant magnets”, to produce radioisotopes
- By accelerating particles at very high speeds, this large machine bombards the stable element with protons to make it radioactive
- We extract the radioisotope, refine it and prepare it for shipment

Types of Cyclotron

Mev	Nuclear Reaction	Modality	Product
13-18	p,n	PET	F-18, 0-15
~30	p,2n p,3n	SPECT	I-123, In-111 Ga-67, Tl-201
70-100	p,4n p,5n	PET	Sr-82/Rb-82
~500	Spallation	PET SPECT	Sr-82/Rb-82 Xe-127

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Medical Radioisotopes

Iodine-123	**Medical Tracing (thyroid, brain, heart, neuroblastoma)**
Thallium-201	**Medical Tracing (heart)**
Gallium-67	**Tracing (soft tissue, abscesses)**
Indium-111	**Medical Tracing (tumours)**
Cobalt-57	**Calibration Sources**
Palladium-103	**Therapy Seeds (prostate cancer)**
Strontium-82	**Medical Tracing**
Copper-64	**Hypoxia**

Characteristics of Medical Radioisotopes

- Radioisotopes have a “shelf life”, called a half life
- Our radioisotopes decay rapidly
  - Example: iodine-123 has a half life of 13 hours
  - Every hour of delay results in a 5% product loss
- Rapid decay = this is a true “just-in-time” business
- Shipping delays lessen its use by the physician (poorer image for diagnosis or needing more to do the same job)

Nuclear Reactions for I-123

$^{124}Xe\ (p,2n)\ ^{123}Cs \rightarrow\ ^{123}Xe \rightarrow\ ^{123}I$

$^{124}Xe\ (p,pn)\ ^{123}Xe \rightarrow\ ^{123}I$

^{123}Cs and ^{123}Xe have half lives of 5.1 minutes and 2.0 hours respectively.

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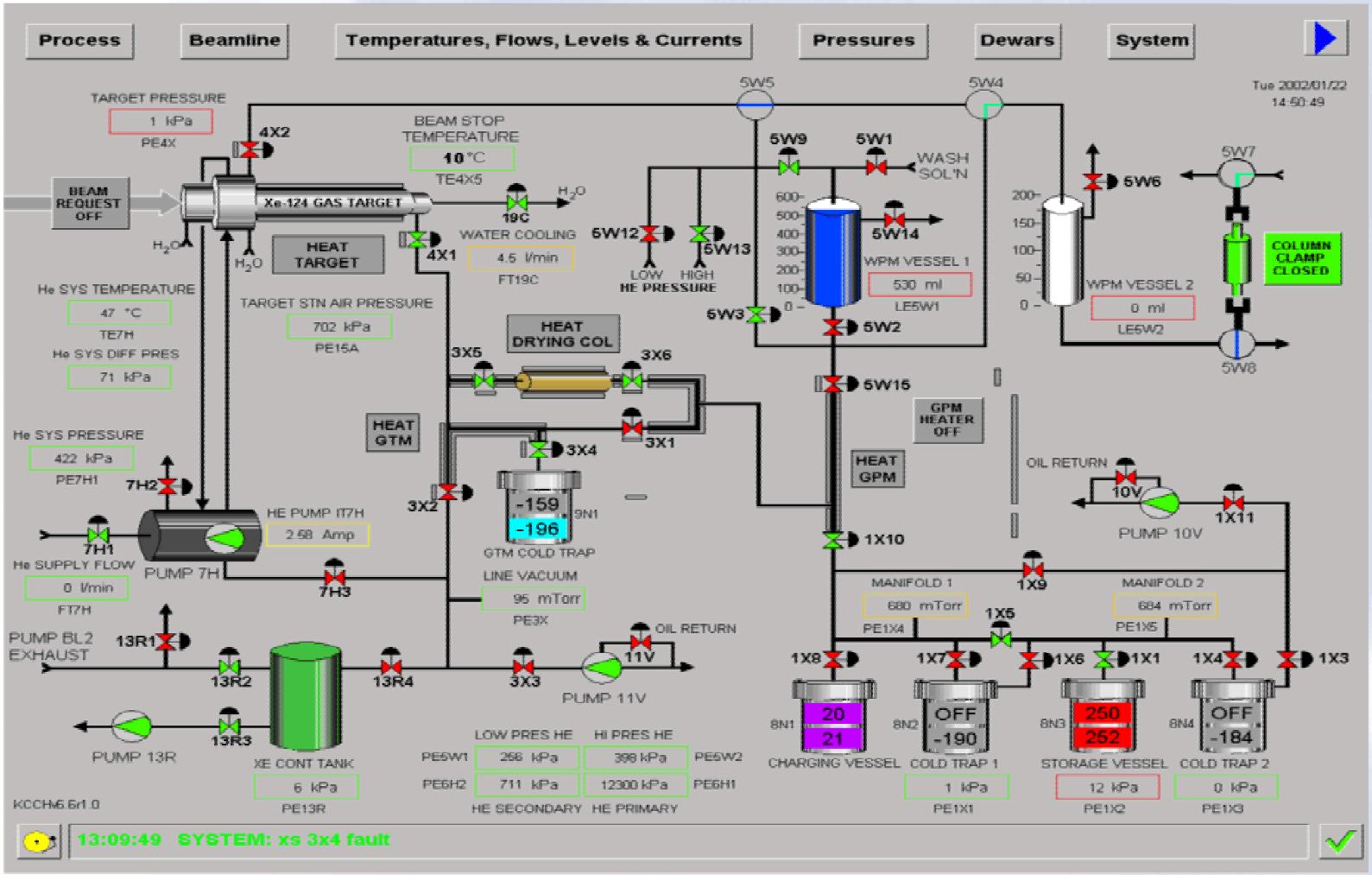
Transferring Xenon-124



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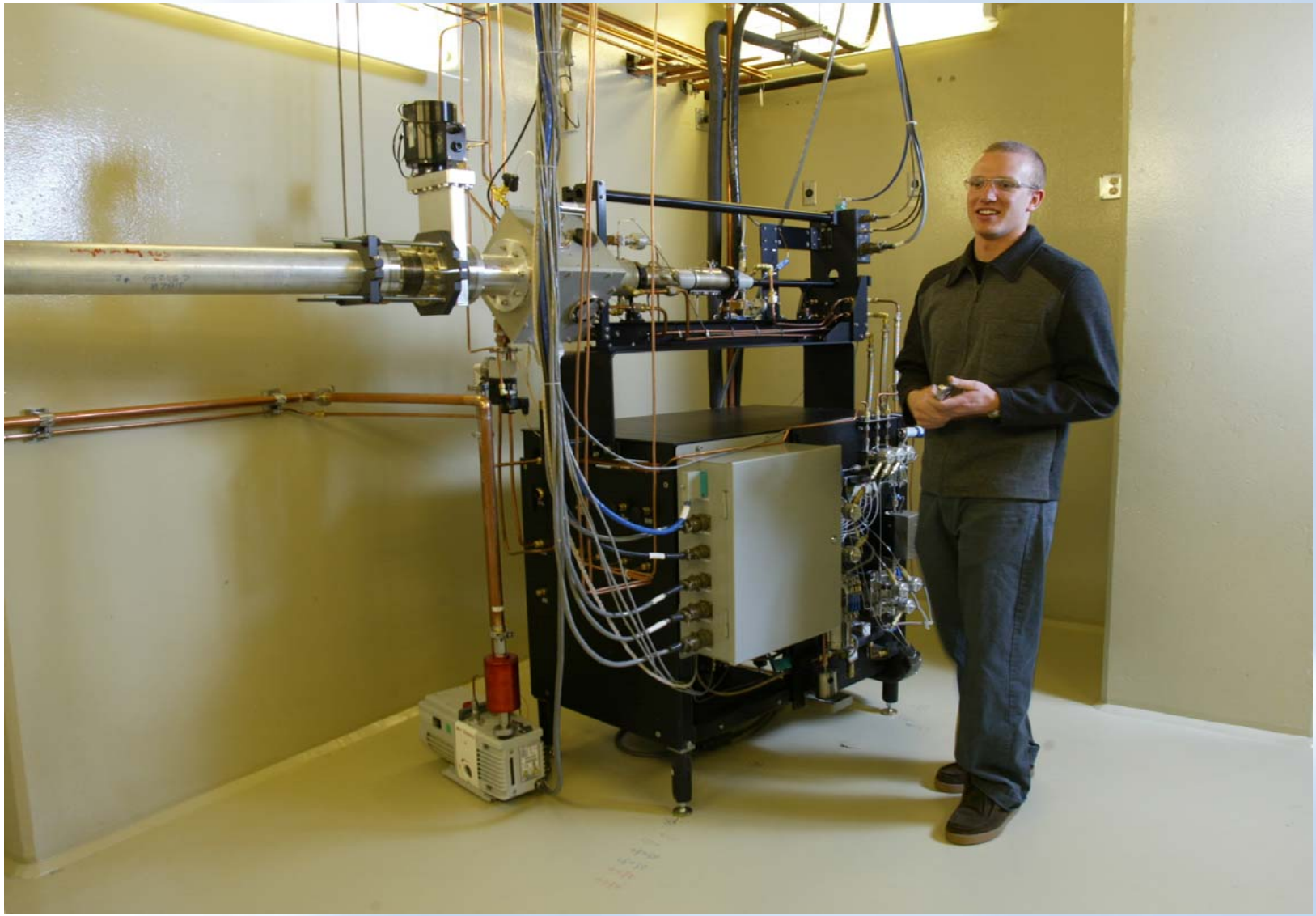
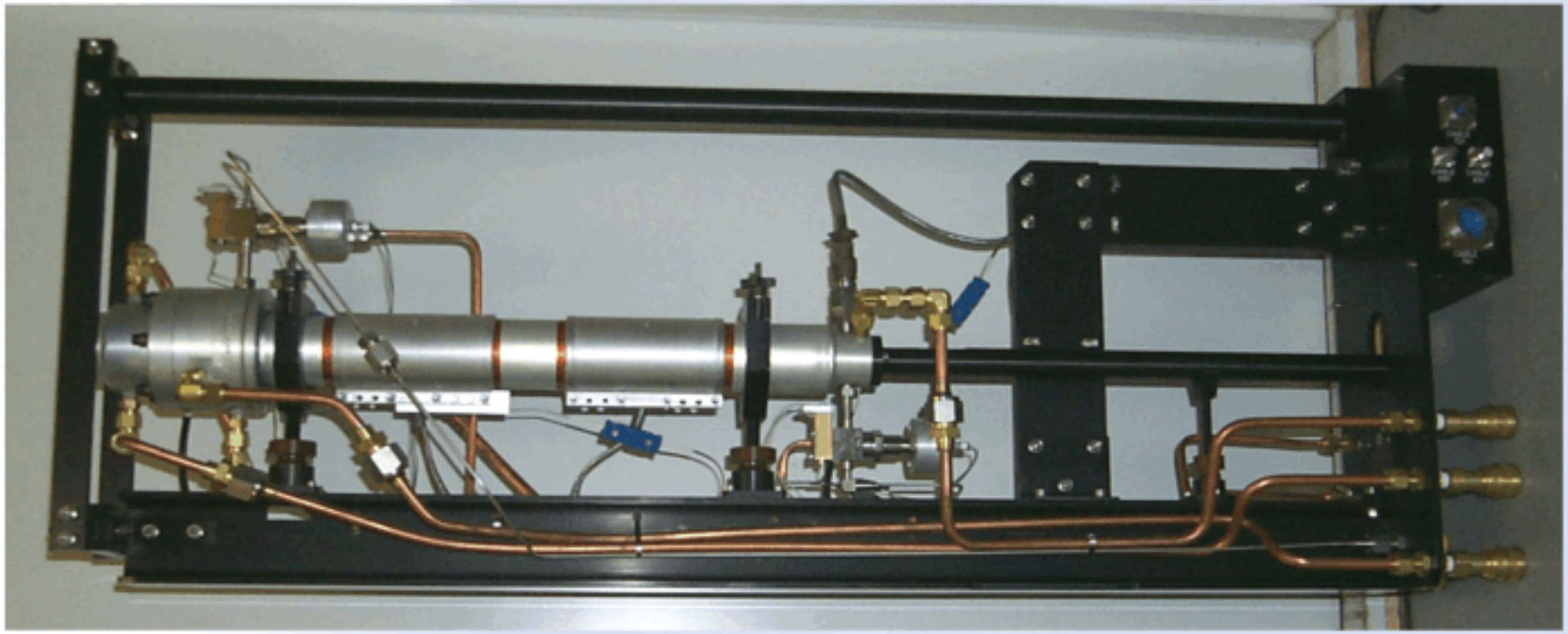


Xenon Gas Target



Xenon gas targets consist of a water cooled Aluminium cylinder with an inside diameter of 2 cm and a length of 50 cm. One end is welded closed with an Aluminium plug and the other end is sealed with two Havar windows and Indium seals. The target is filled with Xenon gas for irradiation.

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Production to Customer Timeline

Day 1

- **0000 PT – Start irradiation of Xenon-124 gas**
- 2200 PT – End of bombardment of Xenon-124 gas

Day 2

- 0500 PT – Processing of Iodine-123
- 0615 PT – Quality Control of I-123
- 0715 PT – Dispensing & Packaging
- 0745 PT – Distribution Documents Completed
- 0800 PT – Transport to Airport
- 0915 PT – Charter to Seattle
- 1015 PT – Customs Clearance & Transfer to Commercial Carrier
- 1230 PT – En-route to Customer
- 1700 PT – Receipt by Customer
- 1800 PT – Manufactured into Capsules

Day 3

- 0800 PT – Use by Patient in Hospital

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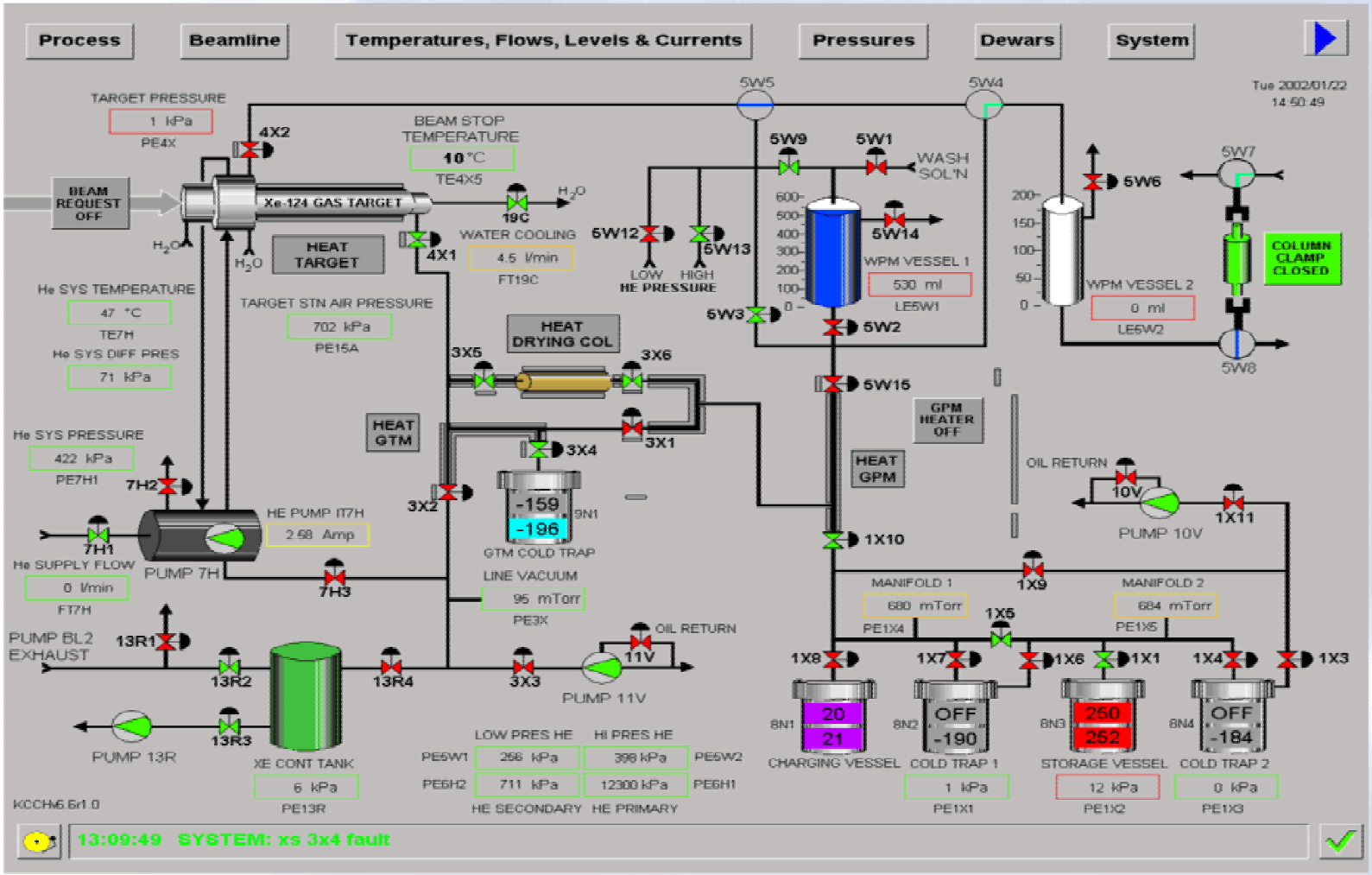

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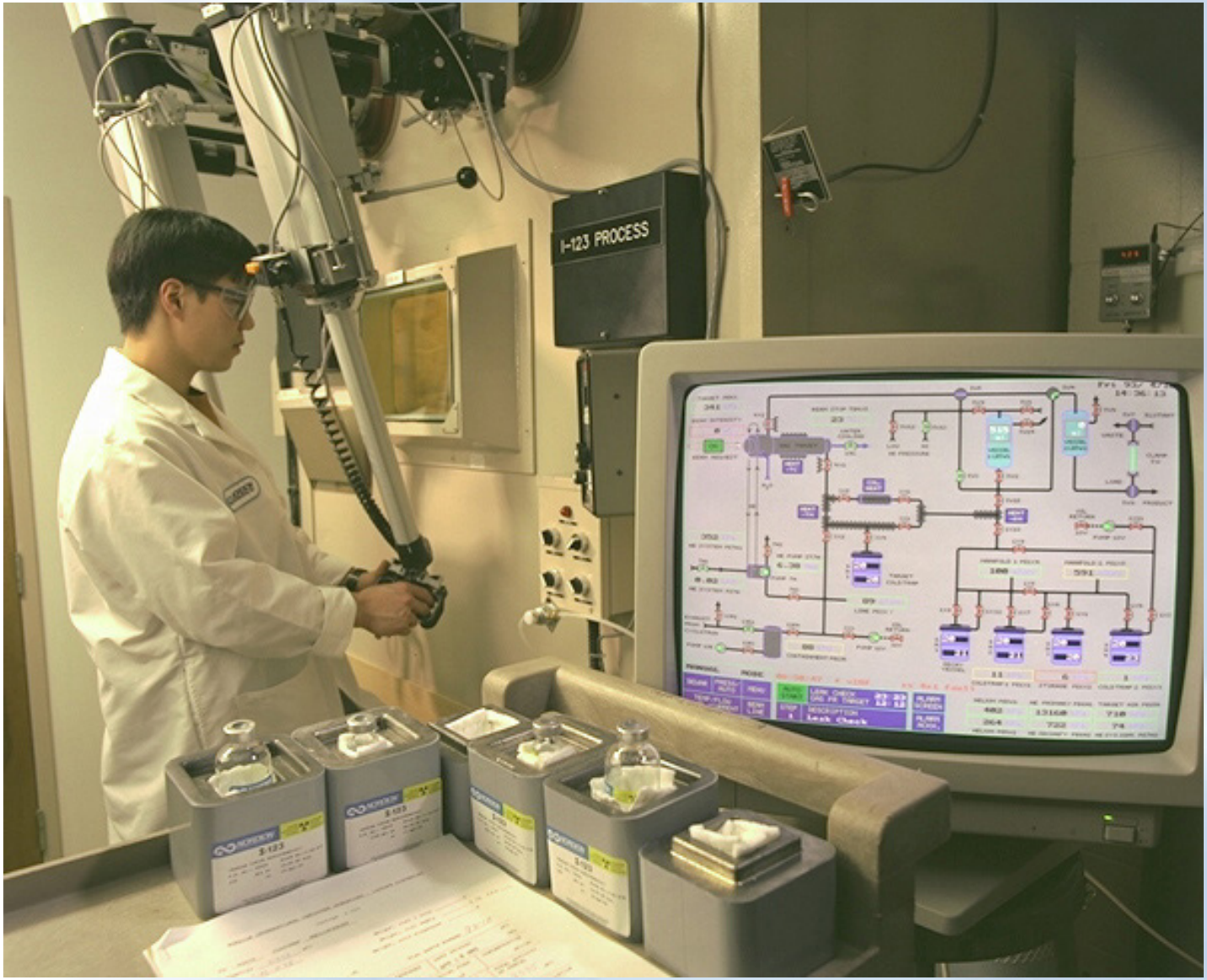
I-123 PROCESS

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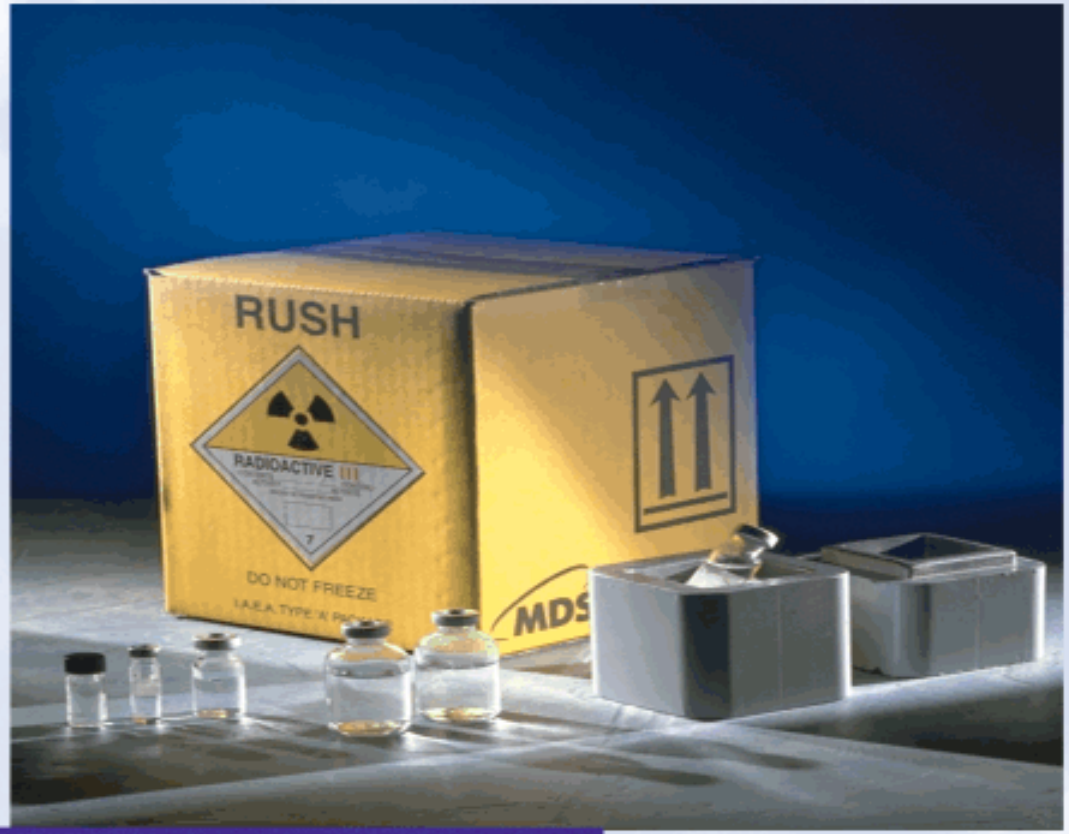
Containers

Ensuring safety and security

- Package safety: all containers are tested, approved/licensed by our regulator, the Canadian Nuclear Regulatory Commission



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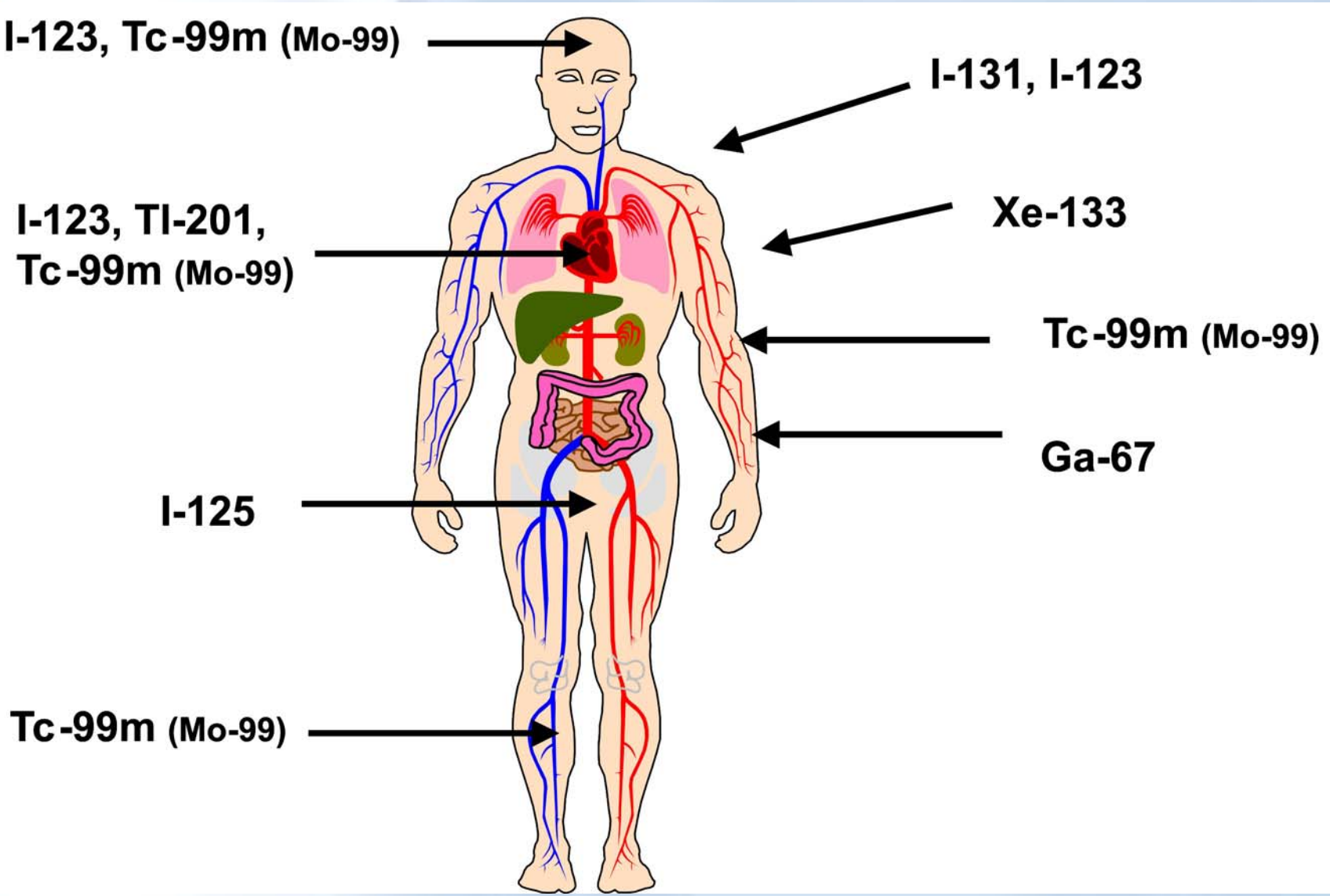
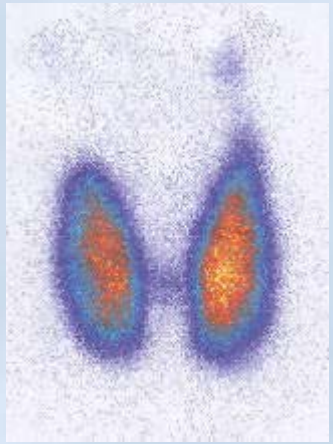
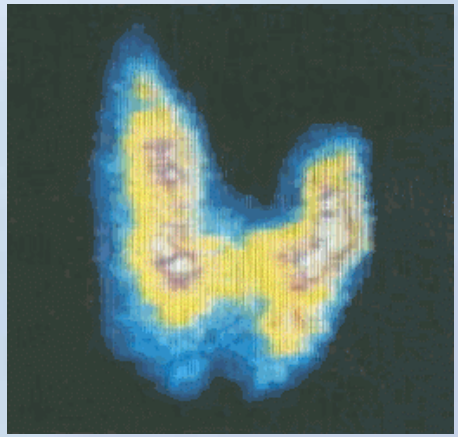

I-123, Tc-99m (Mo-99)
I-131, I-123
I-123, Tl-201,
Tc-99m (Mo-99)
Xe-133
Tc-99m (Mo-99)
Ga-67
I-125
Tc-99m (Mo-99)

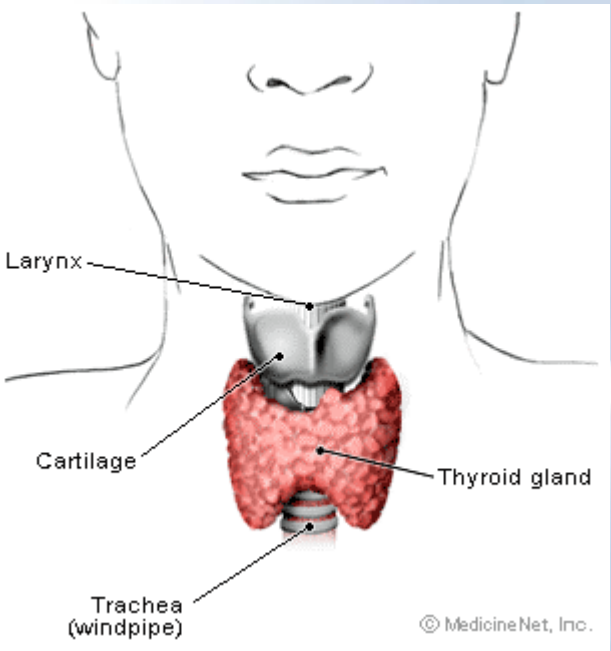
Thyroid scans

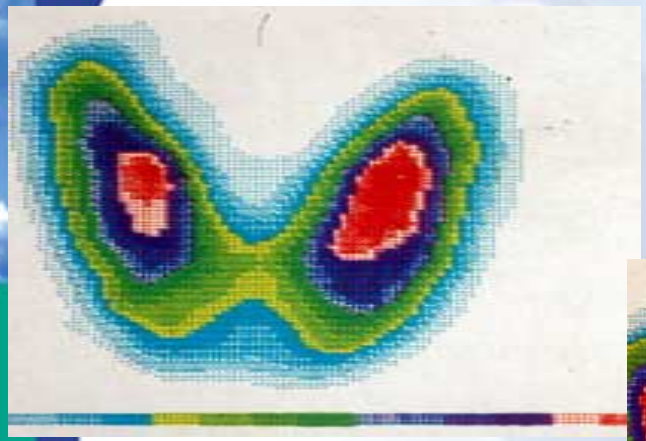
In North America alone, over 8000 people each week undergo a thyroid scan with Vancouver-produced iodine-123. This non-invasive procedure is used to assess thyroid function. Iodine-123 is also an ideal research tool for neurology, oncology and cardiology.

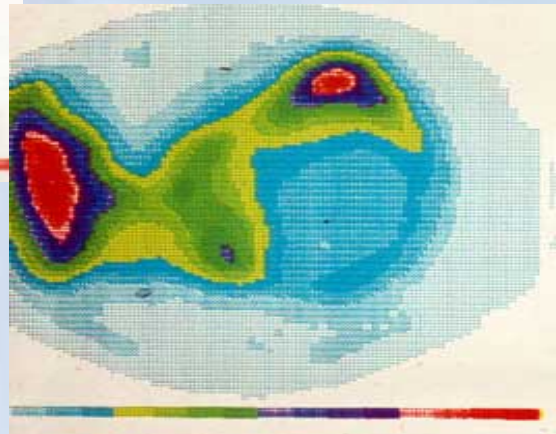


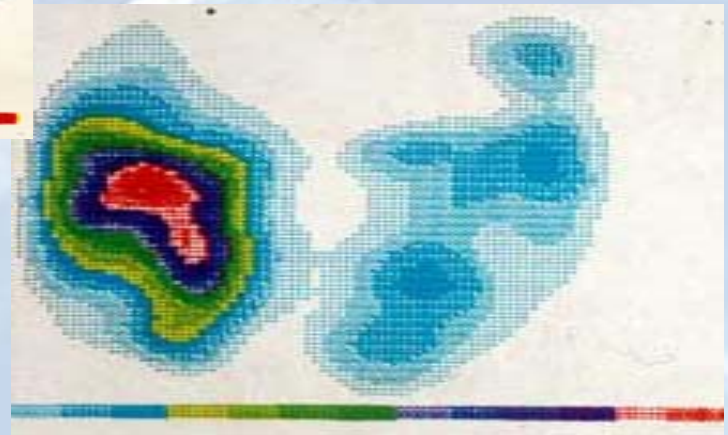


Real scan of radioactive thyroid 24 hours after intake of radioactive iodine



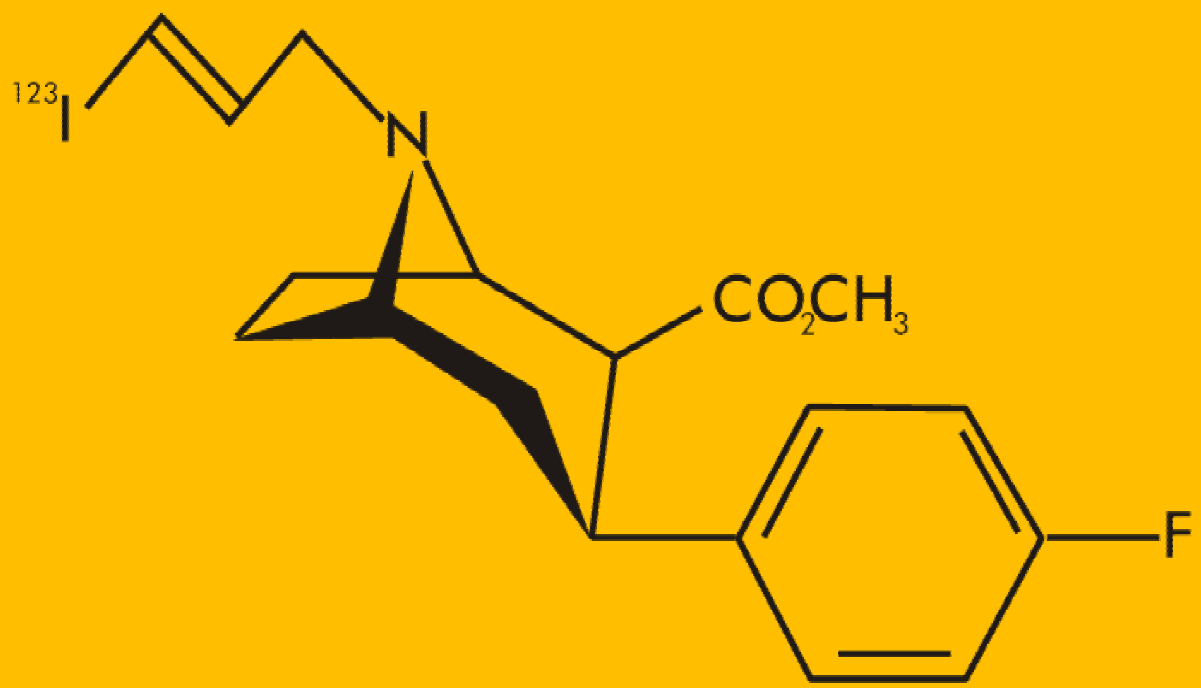






This is a thyroid isotope scan. The first scan shows a normal thyroid gland with two symmetrical lobes and uniform uptake. The middle scan shows a cold nodule in the lower part of the left lobe. The right hand scan shows patchy uptake in the left lobe consistent with multi nodular goitre.

ALTROPANE



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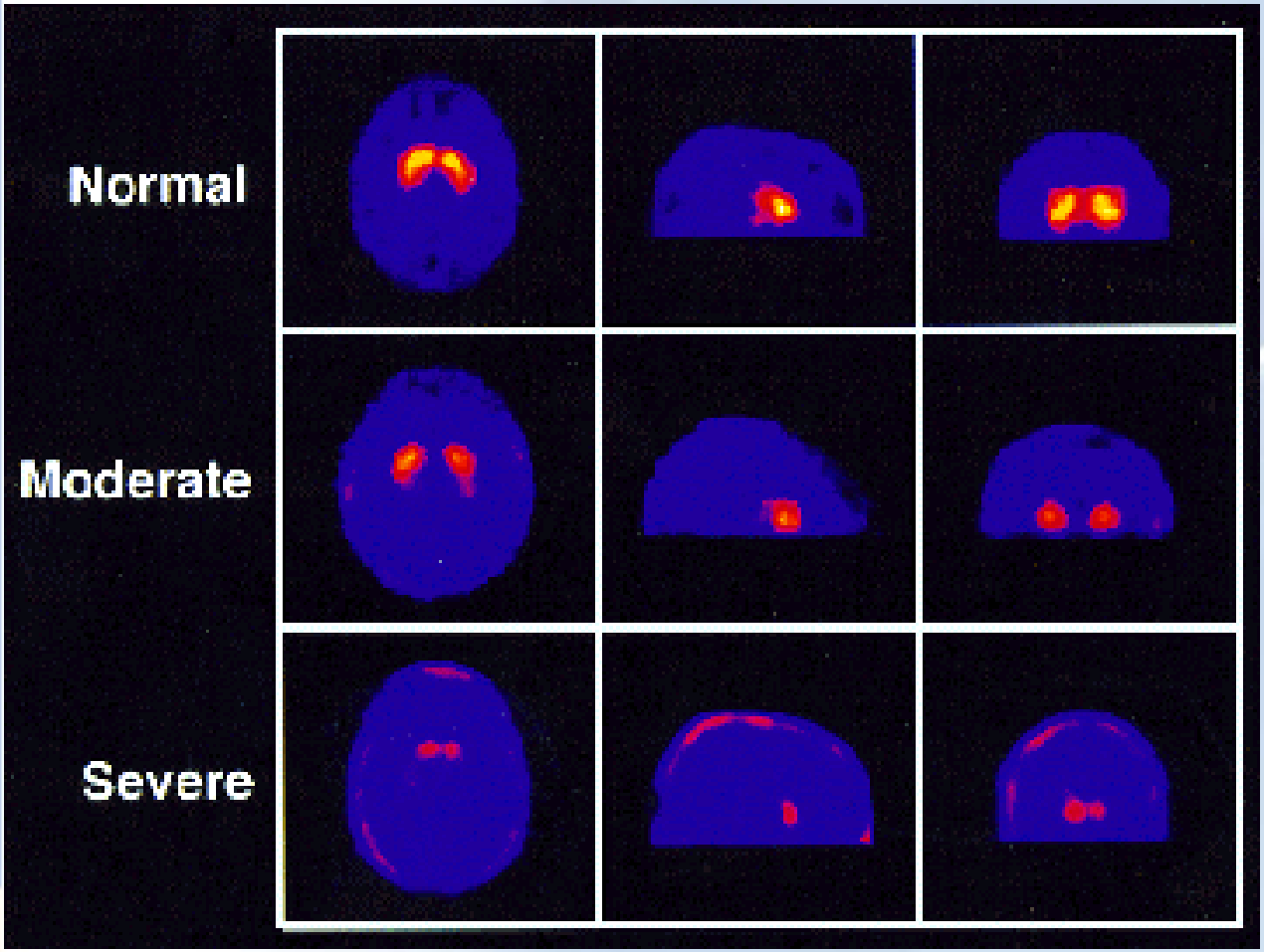
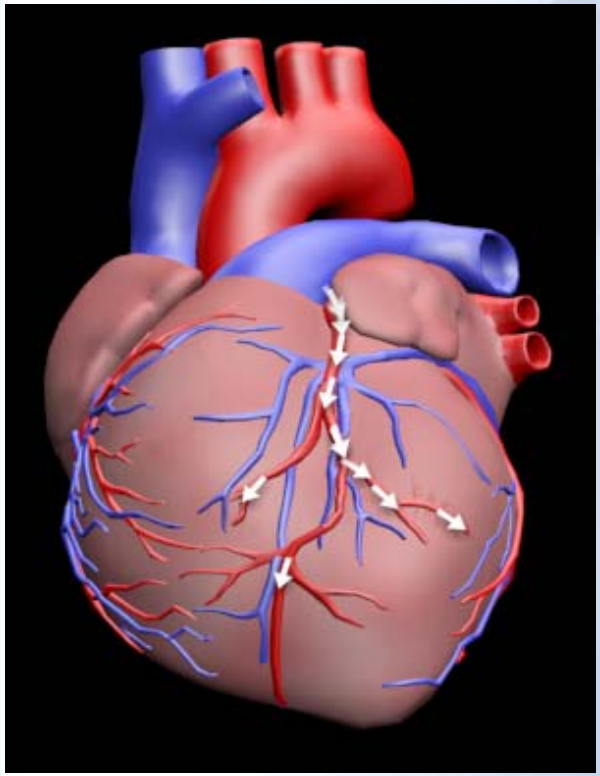
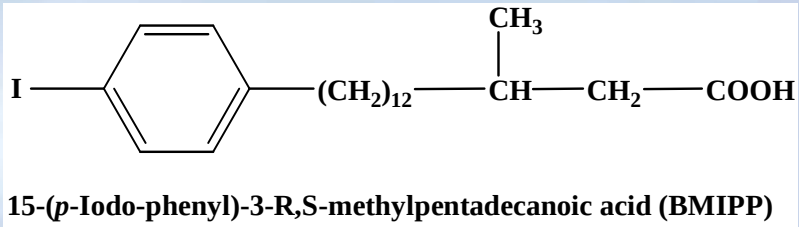


The new imaging agent Altropane visualizes, in healthy people, a crescent-shaped collection of dopamine neurons in the brain's striatum (the yellow and red colored area). In people with Parkinson's, the few remaining neurons yield only a dim signal.

Heart

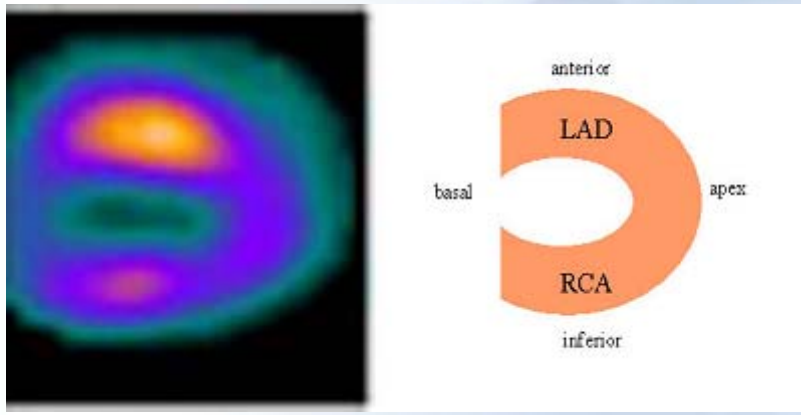


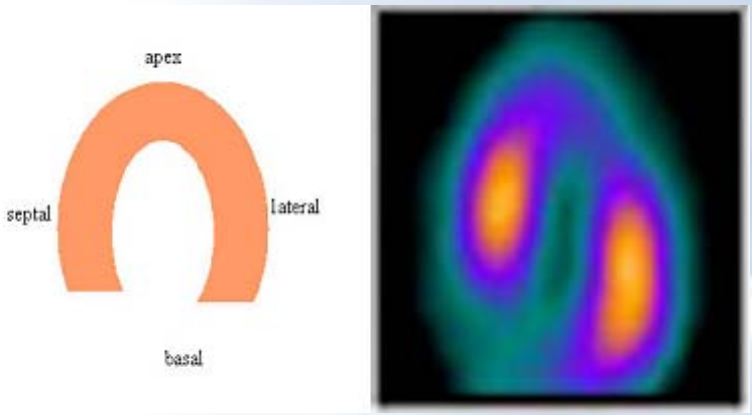


15-(*p*-Iodo-phenyl)-3-R,S-methylpentadecanoic acid (BMIPP)

[^{123}I]-BMIPP

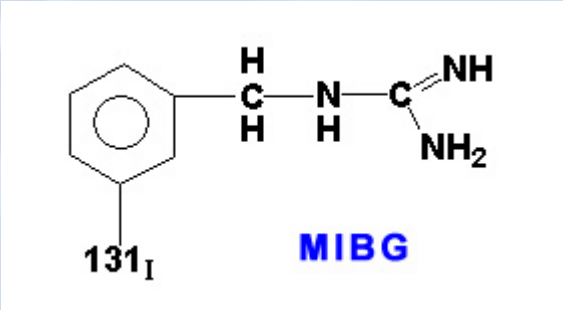
Case Study: 75 year old woman with normal troponin

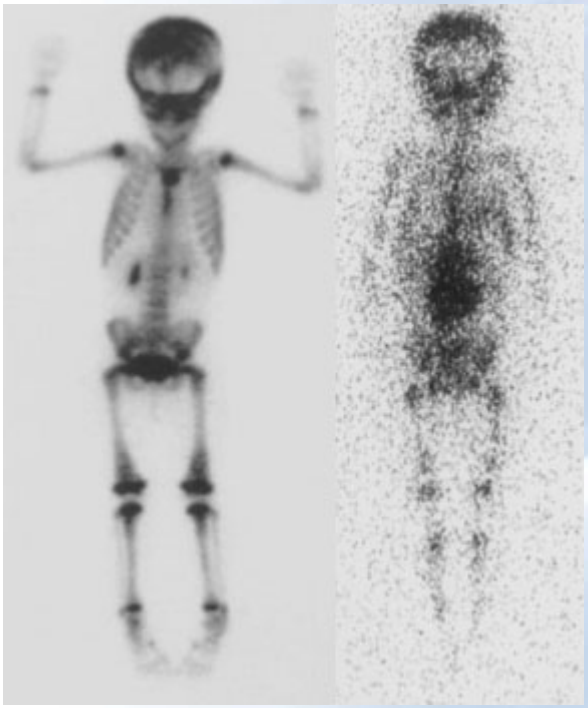




- BMIPP images were taken 10 minutes after injection
- Total study time was 20 minutes
- BMIPP images show an obvious defect in the apex of the heart
- Subsequent troponin 9 hours later confirmed BMIPP result
- Subsequent catheterization confirmed significant coronary artery disease
- Patient received stent
- A non-invasive study in elderly are preferable allowing rapid decision making and reduced risks

Neuroblastoma





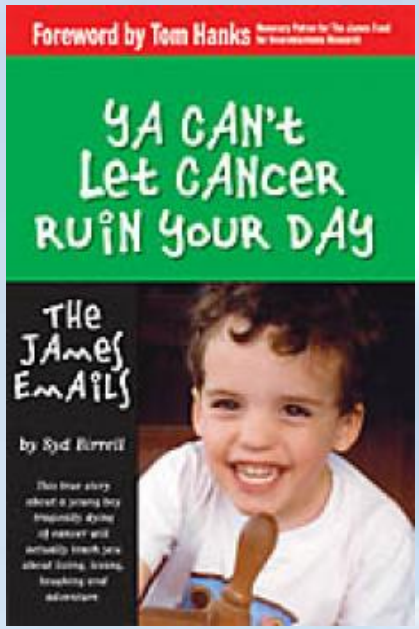
Neuroblastoma: Bone scan and MIBG exam. Diffuse skeletal metastases are evident on bone scan, but are more clearly revealed on the MIBG exam. Uptake within the patients primary lesion can also be seen on the MIBG exam. A plain film skeletal survey demonstrated a very subtle periosteal reaction within the distal left femoral metaphysis, but was otherwise normal

The Story of James Birrell

- 8-year old boy diagnosed with neuroblastoma
- Nordion's I-123 was used for his diagnostic scans
- November 1st, 1993 - December 18th, 2001
- www.jamesbirrell.ca

"Ya Can't Let Cancer Ruin Your Day – The James Emails"

This is a book about a family who chose to make their dreams a reality every day, because they never knew if there would be another day for their young son James as he fought cancer. Some dreams were easy to fulfill (going to the farm, or dinner at the top of the CN Tower) and others were outrageous (Dad, I'd like to drive a freight train that's pulling a hundred cars!), but the result was life lived to the fullest – and an inspirational book called "Ya Can't Let Cancer Ruin Your Day – The James Emails," by Syd Birrell.



Applications of Medical Radioisotopes

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Thallium-201	Medical Tracing (heart)
Gallium-67	Tracing (soft tissue, abscesses)
Indium-111	Medical Tracing (tumours)
Cobalt-57	Calibration Sources
Palladium-103	Therapy Seeds (prostate cancer)
Strontium-82	Medical Tracing
Copper-64	Hypoxia

Reactions for Tl-201

$$^{203}Tl\ (p,3n)\ ^{201}Pb\ T\frac{1}{2}=9.33h\ ^{201}Tl(T\frac{1}{2}=72.9h) \rightarrow\ ^{201}Hg\ (stable)$$

Every year, more than 140,000 people undergo diagnostic tests using Vancouver's thallium-201.

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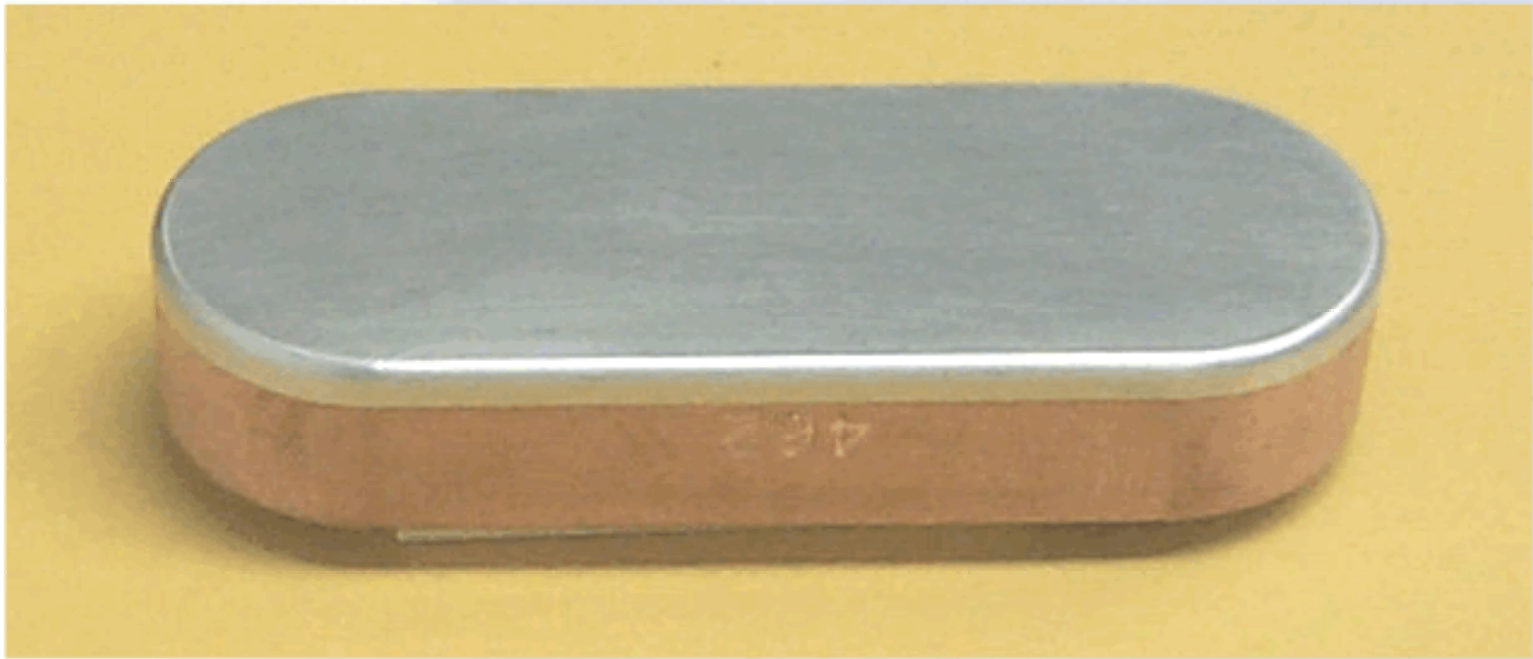
Plated Target



Plated targets, which are Copper backed Silver plates, are approximately 10 cm long and 4 cm wide with rounded ends. The target material is electroplated onto the Silver plate.

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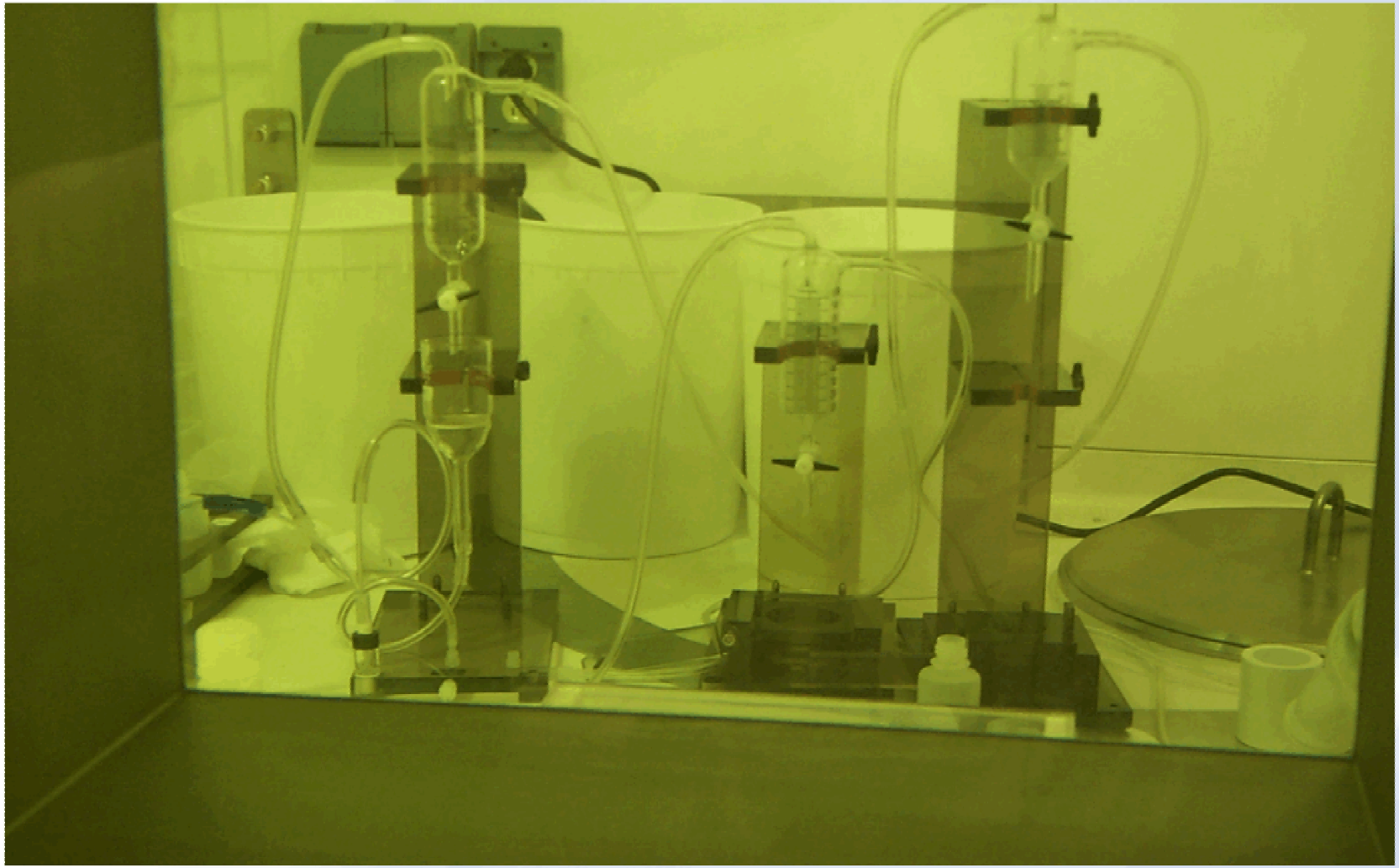
Hotcell Equipment



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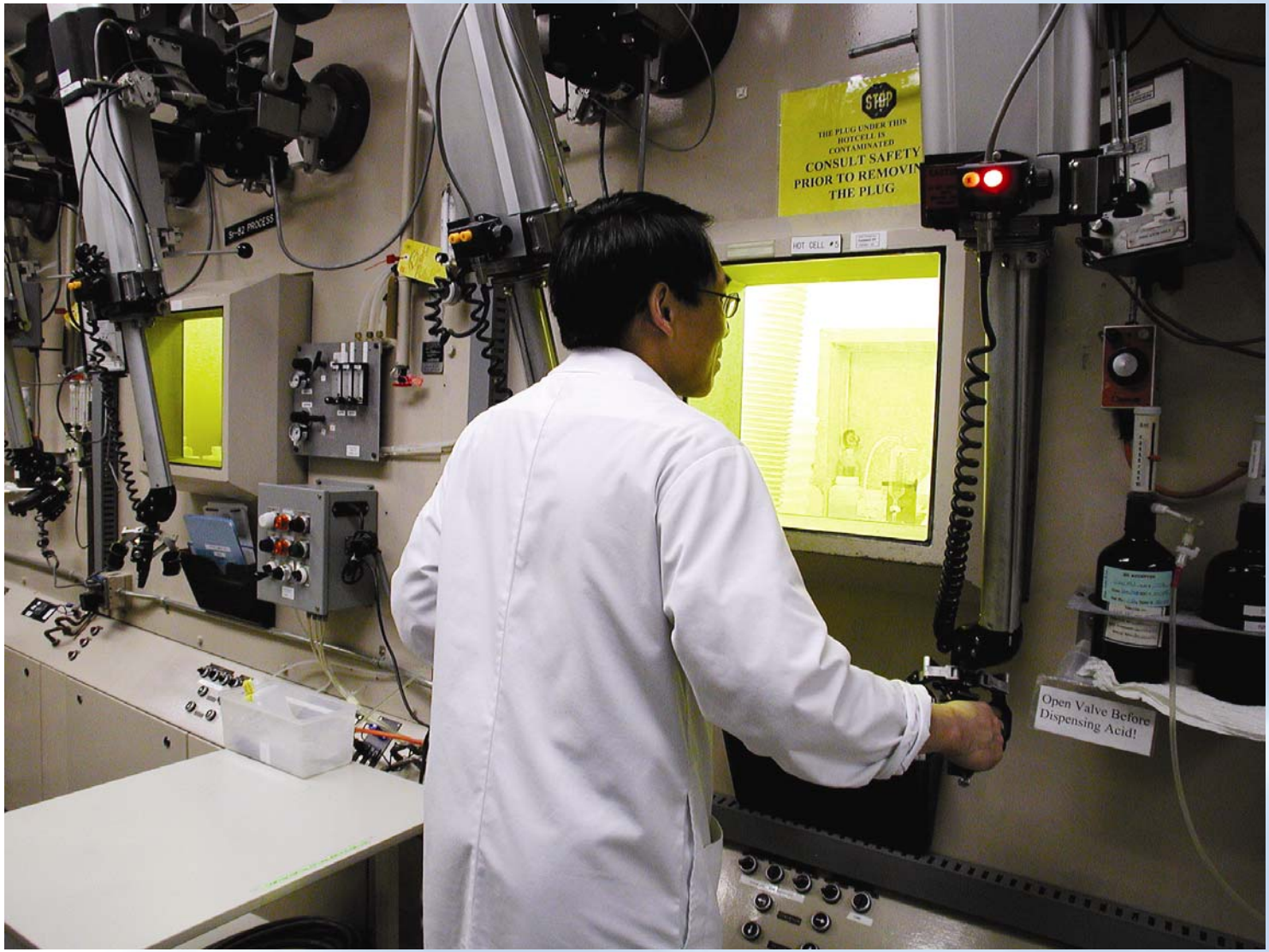
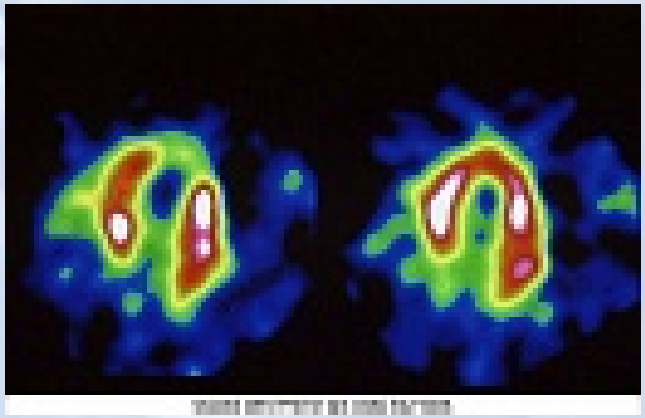
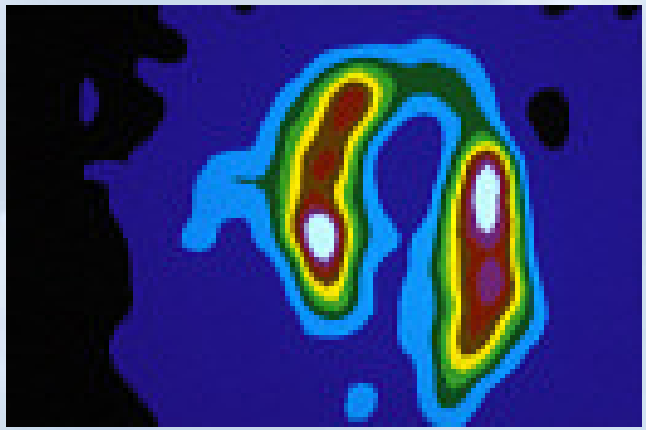

STOP
THE PLUG UNDER THIS
HOTCELL IS
CONTAMINATED
CONSULT SAFETY
PRIOR TO REMOVIN
THE PLUG
S-02 PROCESS
HOT CELL #5
Open Valve Before
Dispensing Acid!



Scintigram using Thallium 201 of myocardial infarction, which is the formation of an occlusion of the arterial supply or venous drainage in the middle and thickest layer of the heart wall.

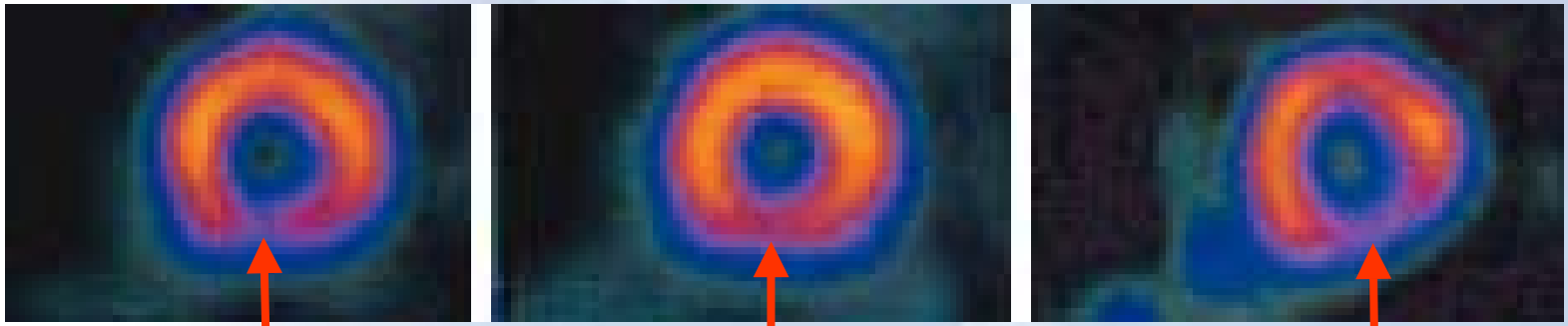


Thallium Blood Flow

Stress | Rest

BMIPP

Rest



Ischemic area detected after 20 minutes of exercise

Fill-in 3 hours later shows viable heart muscle

Decreased fatty acid metabolism shows “ischemic memory” 10 min after injection of BMIPP and 5 hours after stress

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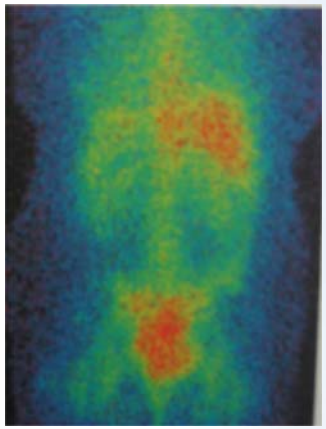
Nuclear Reactions for Ga-67

$$^{68}\text{Zn (p, 2n)} \longrightarrow {}^{67}\text{Ga}$$



Gallium-67 is used for imaging various tumours such as Hodgkin's disease and lymphoma. Every year, the gallium-67 from Vancouver is used to perform 87,000 scans on patients in Europe and South America.

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Gallium-67 Scans

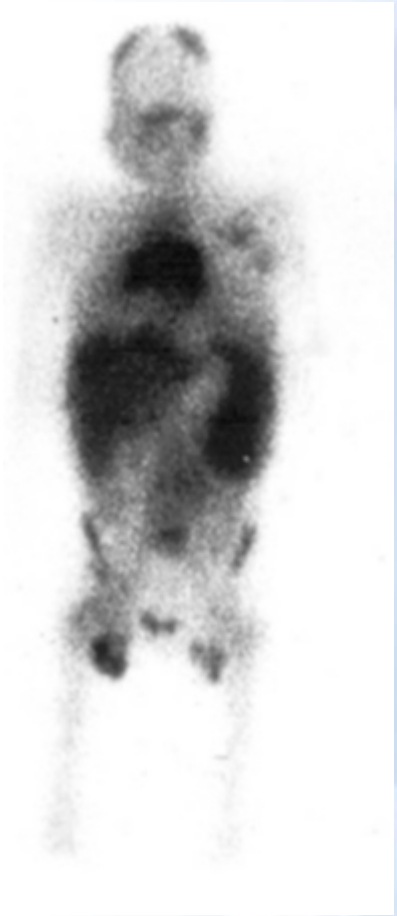

Figure 1. Whole-body gallium-67 scan showing lymphoma in the chest, the spleen, the abdomen, and the groin. The chest and spleen sites were known before the scan. The abdominal and groin uptakes were detected only by the scan.

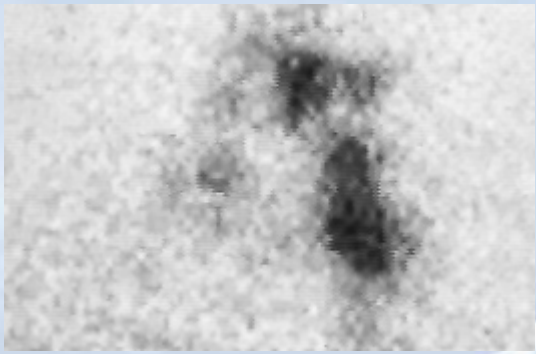

Figure 2. Gallium-67 scan over the chest region showing uptake in mediastinum (center of the chest) and lining of the heart (pericardium). This pericardial uptake was not seen on other tests. The scan represents lymphoma at both these sites.

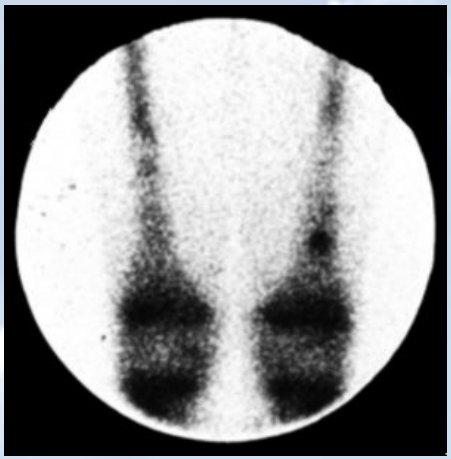

Figure 3. Gallium-67 scan showing uptake in the left femur (dark area) just above the knee. The involvement of bone means that Stage IV disease is present and more aggressive therapy is required.

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Cobalt-57	Calibration Sources
Palladium-103	Therapy Seeds (prostate cancer)
Strontium-82	Medical Tracing
Copper-64	Hypoxia

Nuclear Reactions for In-111

$$^{112}Cd\ (p, 2n) \rightarrow\ ^{111}In$$

Indium-111 is used in the labelling of antibodies and other substances for imaging, and is being investivated for a therapeutic application.

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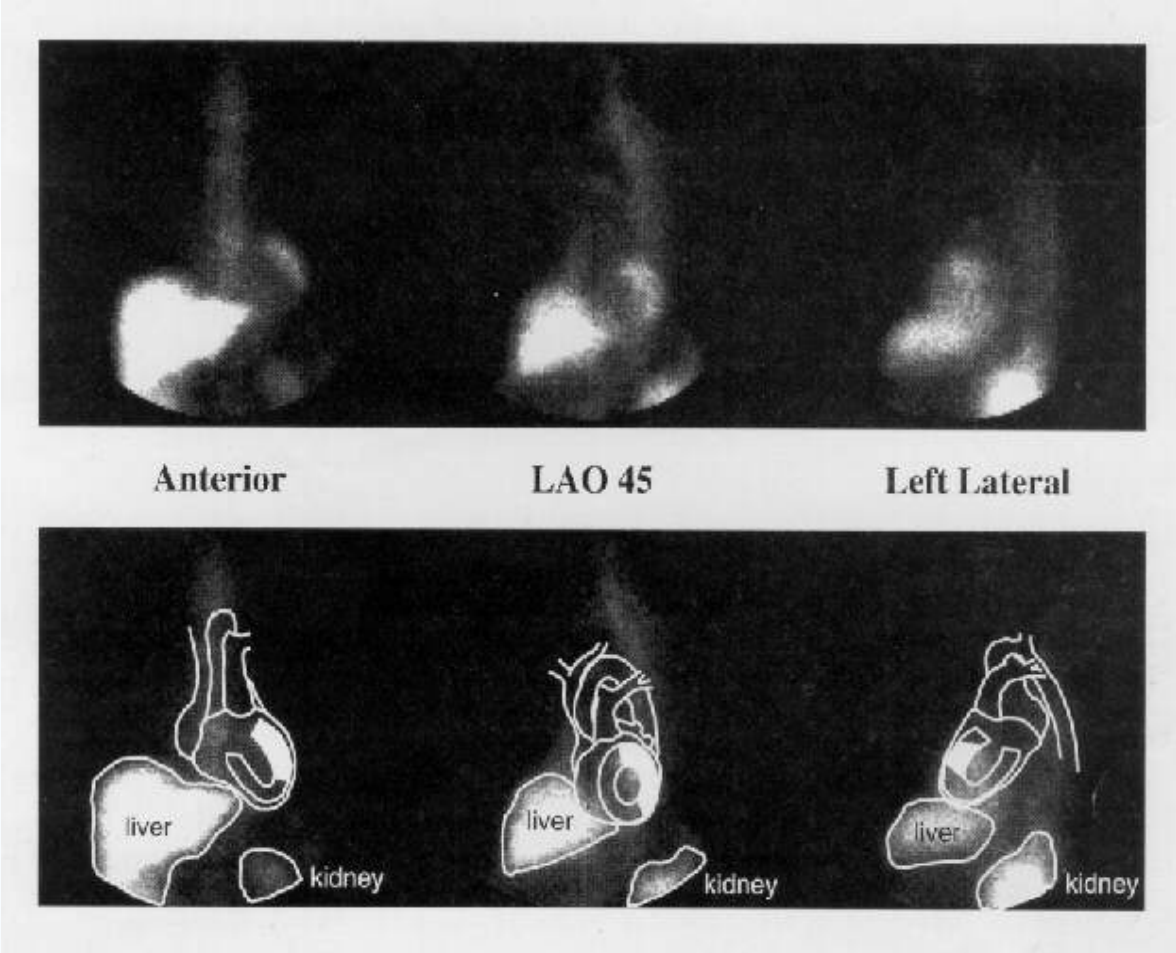


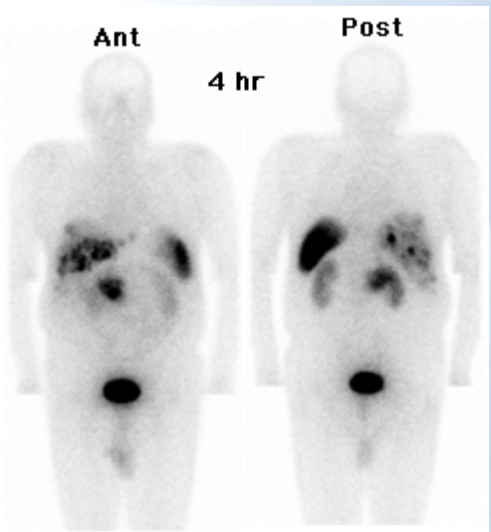
Indium-111 antimyosin images showing increased uptake in the lateral wall (panel A) in a patient with recent acute lateral myocardial infarction.

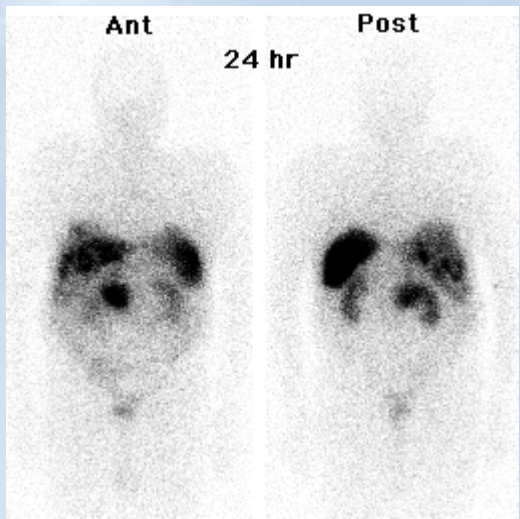
Somatostatin Receptor Imaging
Gabriel Soudry, M.D.
Kevin J Donohoe, M.D.

May 30, 1995

Case Presentation:
A 62 year-year-old man presented with severe diarrhea, weight loss and increased flatulence. On exam he was icteric and had a palpable gallbladder.
Abdominal revealed a mass in the head of the pancreas measuring 4 X 4.5 X 3 cm. No abnormalities were demonstrated in the liver, adrenals or spleen.
The total bilirubin was 5.2.
An exploratory laparotomy showed liver metastasis.
A cholecystojejunostomy was performed.
The tumor cells showed no staining for insulin, glucagon, somatostatin or gastrin.
The final pathologic diagnosis was metastatic neuroendocrine carcinoma.
One month after the surgery, an Indium-111-Pentetreotide (Octreoscan(R)) study was obtained. Three weeks later, a repeat abdominal CT was performed.

Findings:
An Indium-111-Pentetreotide scintigram was obtained 4 hours and 24 hours after injection. There was intense increased tracer localization in the pancreatic mass and multiple abnormal foci of uptake throughout the liver consistent with diffuse liver metastases.





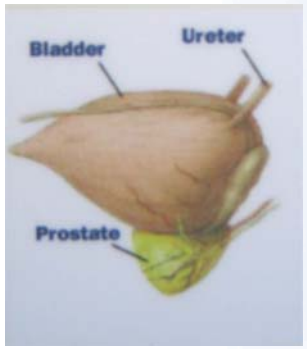
Ref: http://www.med.harvard.edu/JPNM/TF94_95/May30/WriteUpMay30.html

Applications of Medical Radioisotopes

Iodine-123	**Medical Tracing (thyroid, brain, heart, neuroblastoma)**
Thallium-201	**Medical Tracing (heart)**
Gallium-67	**Tracing (soft tissue, abscesses)**
Indium-111	**Medical Tracing (tumours)**
Cobalt-57	**Calibration Sources**
Palladium-103	**Therapy Seeds (prostate cancer)**
Strontium-82	**Medical Tracing**
Copper-64	**Hypoxia**

Nuclear Reactions for Pd-103

$$^{104}Pd \xrightarrow{p,pn} {}^{103}Ag \xrightarrow{1.0\ hrs} {}^{103}Pd$$



In North America, a man is diagnosed with prostate cancer every three minutes on average. Fortunately if detected early, this is one of the easiest malignancies to treat and a growing number of people are being treated with palladium-103 produced at Vancouver Operations.

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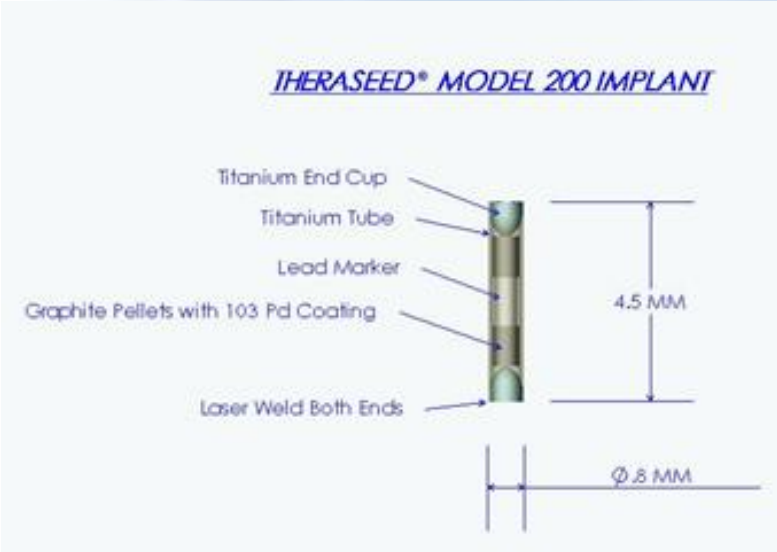
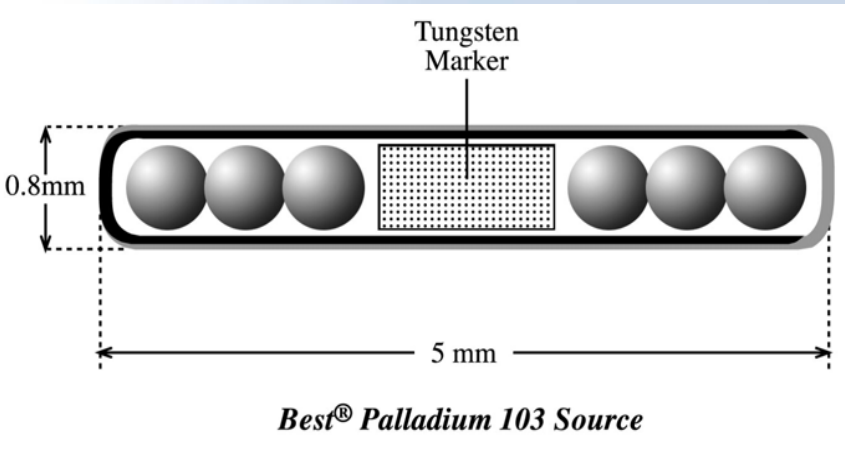
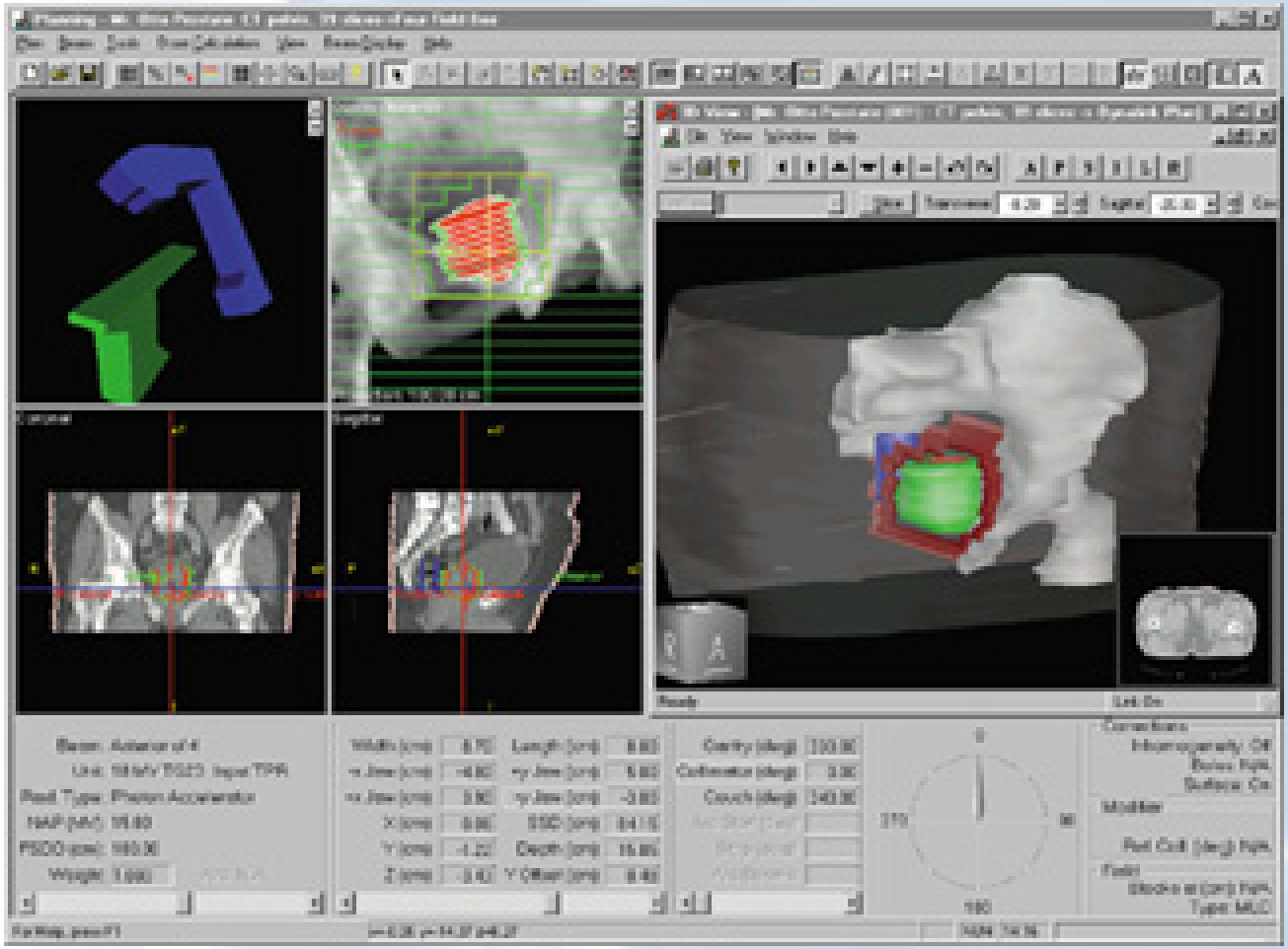


Theragenics Corp.



Best Medical International

North American Scientific



Ultrasound image of prostate

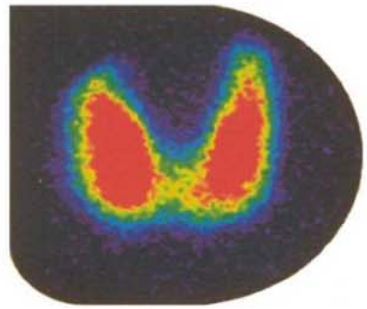
MDS Nordion
Science Advancing Health

TRIUMF

25 years of Industry/Academic/Research Partnership

Products:

Iodine	-123	(thyroid)
Thallium	-201	(heart)
Indium	-111	(abscesses)
Palladium	-103	(prostate)



45,000 patients per week receive radioisotopes produced by our cyclotrons

Future:

Growing demand for Nuclear Medicine radioisotopes both diagnostic & therapeutic

2004 Recipient of the NSERC Synergy Award for Innovation: MDS Nordion & TRIUMF

MDS
Science advancing health

Thank you!

From all of us at Vancouver Operations!