Future Needs for Standards in ^{90}Y Microsphere Therapy

CIRMS 2012

Reed Selwyn, PhD, DABR

24 October 2012

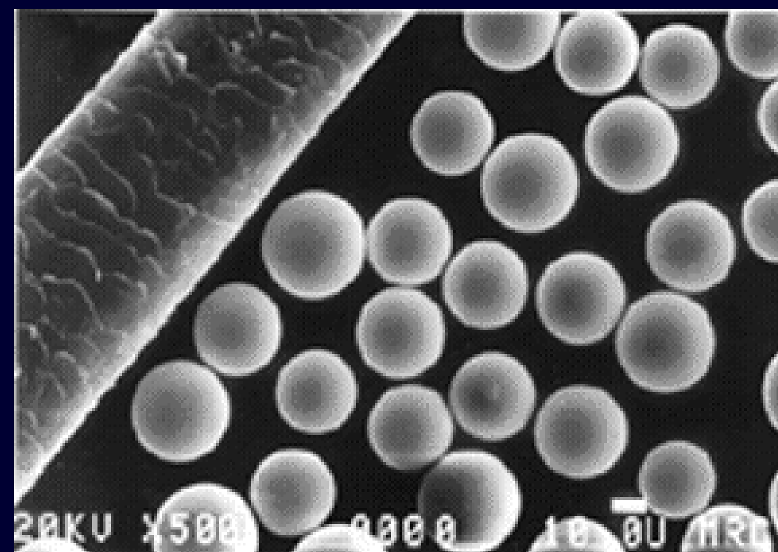
UNIFORMED SERVICES UNIVERSITY
of the Health Sciences

Objectives

I. General Description
- Microsphere Distribution
- Product Comparison

II. Dosimetry Models
- Shortcomings

III. Uncertainty Analysis
- Y90 Assay
- Activity Injected
- NIST Standards and Needs



Human hair compared to Therasphere

Liver Cancer

- Two types of liver cancer
  - Hepatocellular Carcinoma (HCC) = Primary
    - 28,720 new cases estimated for 2012 (ACS)
    - Resectable → curative
  - Hepatic Metastasis = Secondary
    - Colorectal – 150,000 cases estimated for 2006
    - Others
    - Nonresectable → palliative
- Microspheres approved for HCC and colorectal liver metastasis

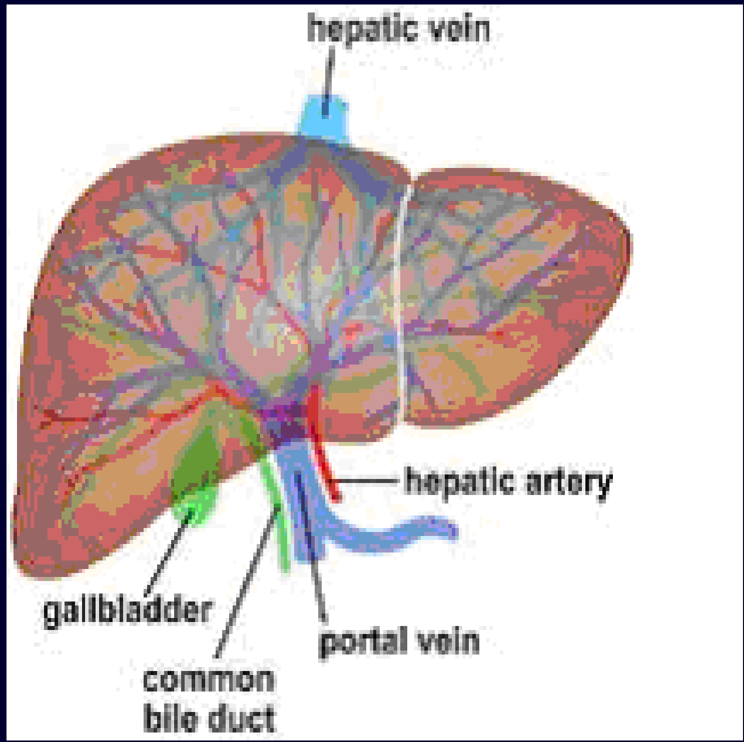
I. General Description

- How does the treatment work?
  - ^{90}Y-loaded microspheres
  - Insoluble device
    - 15 – 40 μm diameter
    - ^{90}Y β emitter ($t_{1/2}$ = 64 h)
      - E_{max} = 2.28 MeV
      - E_{ave} = 0.93 MeV
      - X_{90} = 5.3 mm

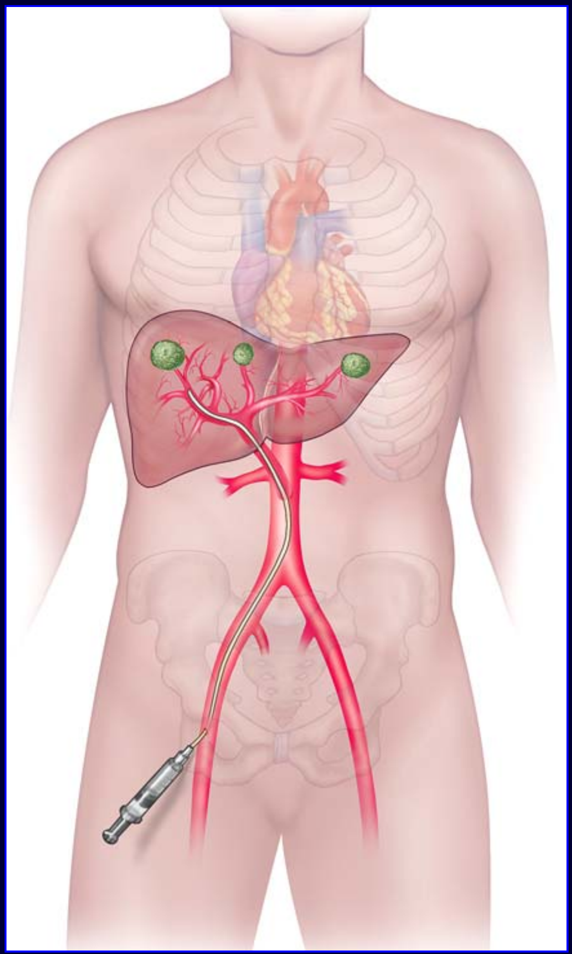
  - Injected via the femoral artery to the hepatic artery by the IR
  - Spheres preferentially deposit in tumors

Liver Blood Flow

- Normal supply
  - Hepatic artery → 20%
    - From celiac trunk
    - Oxygenated
  - Portal vein → 80%
    - From GI tract
    - Venous blood - branches
- Tumor supply
  - Hepatic artery → 80%
  - Portal vein → 20%

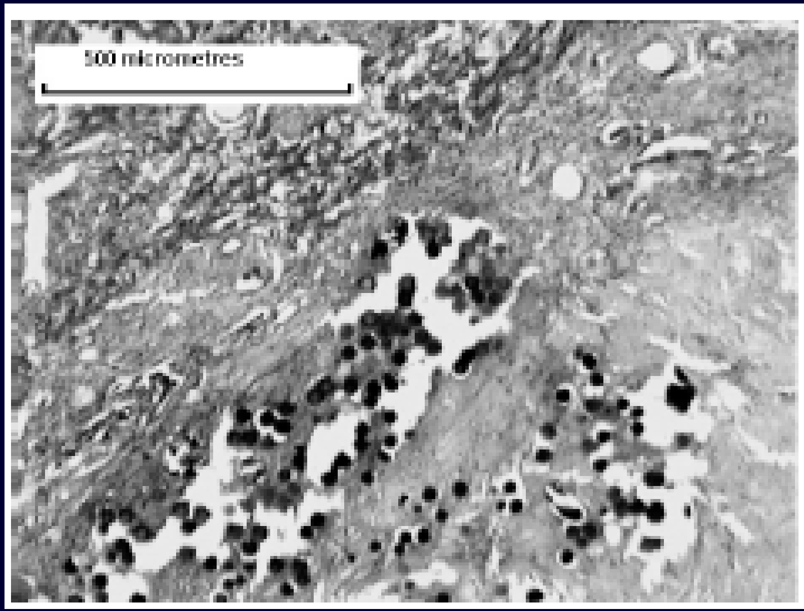


Patient Injection & Delivery Box



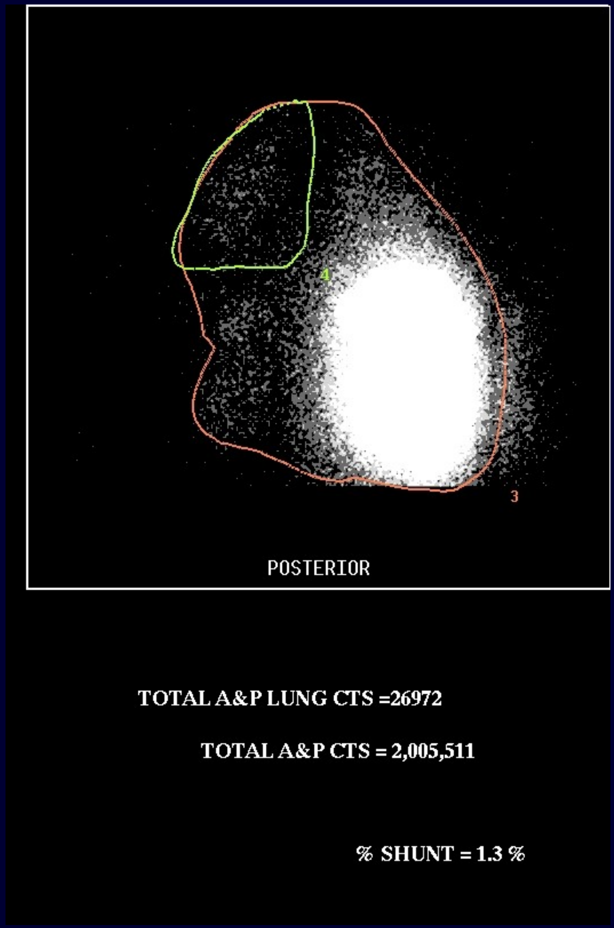
Microscopic Distribution

- Non-uniform sphere dist.
  - Spheres cluster
    - 1 – 20 spheres/cluster
    - Cluster extent of 0.5 – 1 mm
  - Tumor periphery
    - Surface = 175 spheres/mm^3
    - Core = 2.7 spheres/mm^3
  - Nontumorous tissue
    - 3.5 spheres/mm^3
- Tumor to Normal Ratio (T:N)
  - Range from 1:1 to 200:1



In Vivo Assessment of Distribution

- ^{99}Tc-labeled Macroaggregated Albumin (MAA) scan
  - Particle Size: 10 – 100 um
  - Degradeable
    - Particle size < 10 um
    - Inaccurate flow analysis
  - % Lung Shunt
  - Prescan
- CT Scan



Product Comparison

	Therasphere® (MDS, Nordion)	**SIR-Spheres®** (SIRTex)
Size	15-35 um	20-40 um
Material	Glass (3.2 g/cc)	Resin (1.6 g/cc)
Specific Activity	2500 Bq/sphere	50 Bq/sphere
# of spheres injected	1.2 – 20 million	20 – 60 million

II. Dose Estimation Models

- Intraoperative beta dosimetry
  - Direct measurement
    - Beta probe swept over liver surface
    - Determine mean count rate (cps)
    - Determine mean activity
      - Assume homogeneous sphere distribution
    - Calculate liver dose
  - Invasive
  - Difficult application to metastatic cancer

Dose Estimation Models Cont'd

- MIRD Formalism
  - Assumptions:
    - Homogeneous distribution in source (liver)
      - No distinction between normal liver and tumor
    - No dose to non-source organs
      - $\Phi = 0$ for target for beta emitting source
  - Overestimates dose to normal liver
  - Underestimates dose to tumor

$$\overline{D} = \frac{\tilde{A}}{m_l} \sum_i \phi_i (r_k \leftarrow r_h) \Delta_i$$

Dose Estimation Models Cont'd

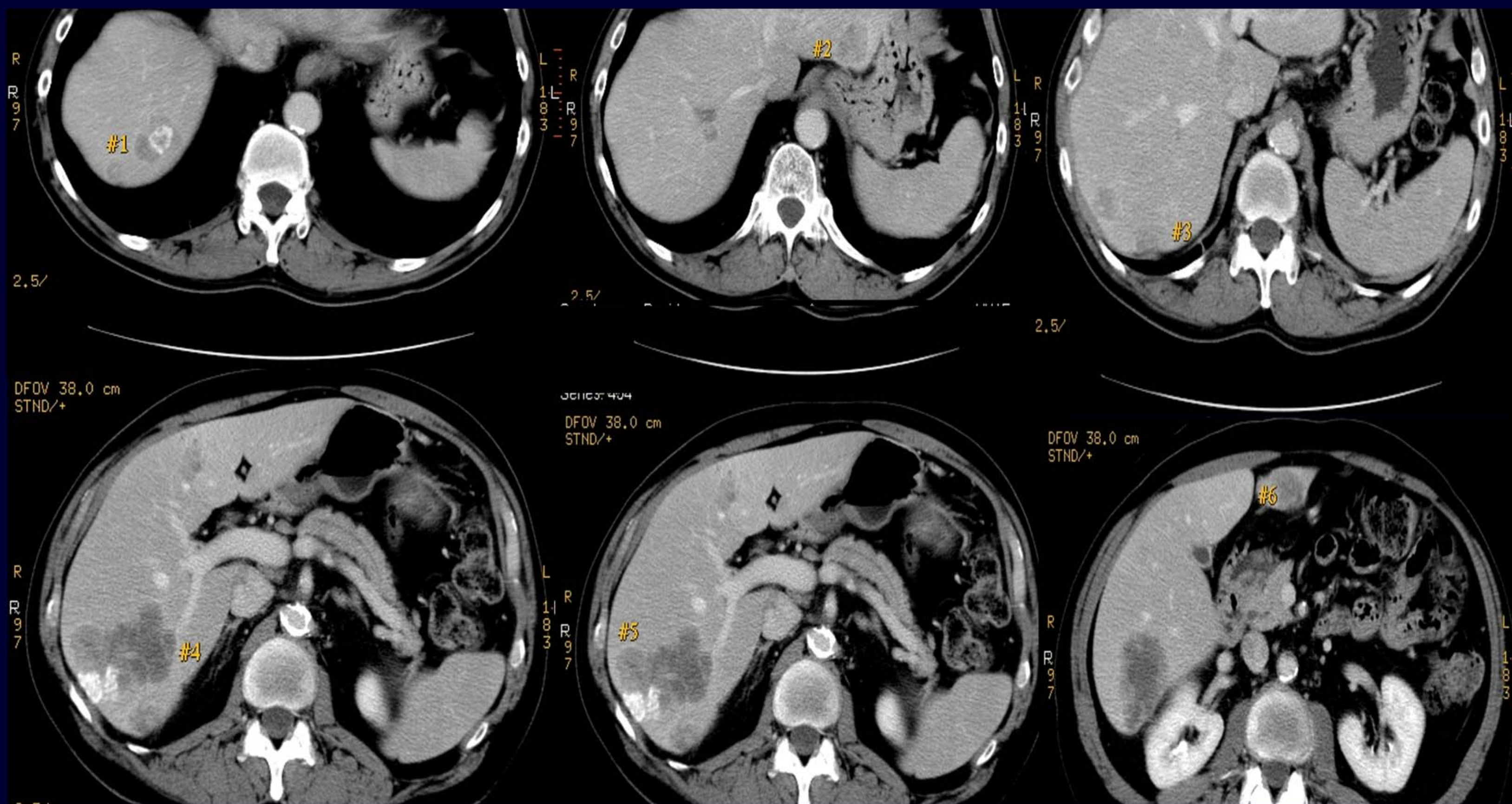
- Partition Model
  - Determine tumor-to-normal tissue ratio (T:N)

$$T:N = (A_t / M_t)/(A_l / M_l)$$

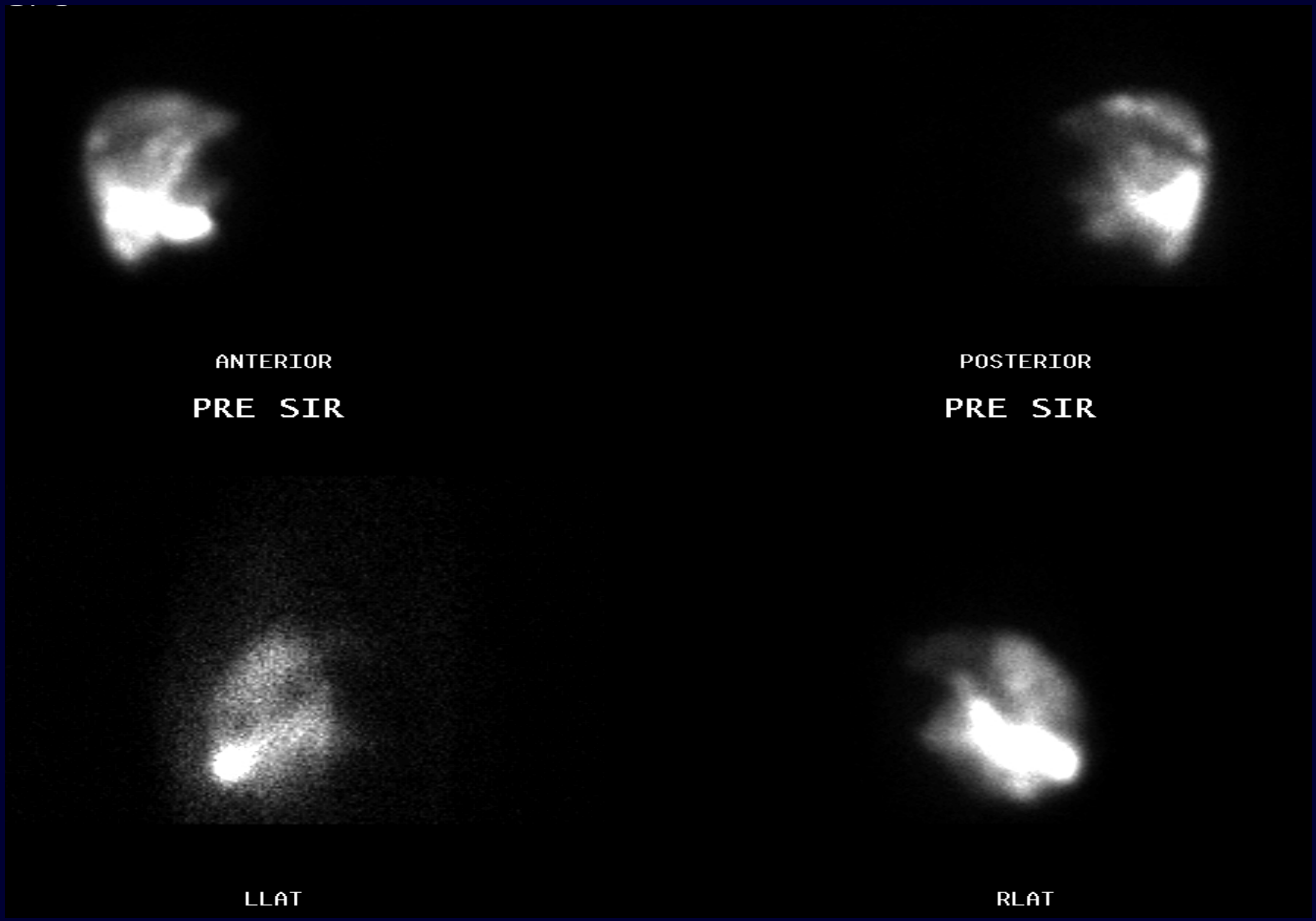
$$D_{liver} = \frac{50 Gy \cdot kg}{GBq} \frac{A_{inj}(1 - F_{lung})}{(T:N)M_t + M_l}$$

    - Evaluate compartment activity and mass
      - Based on ^{99m}Tc-MAA prescan
    - Still assumes no dose to normal tissue from tumors
  - Application to metastatic cancer
    - Difficult to determine tumor mass and uptake fraction

Determination of Tumor Mass



T:N Ratio

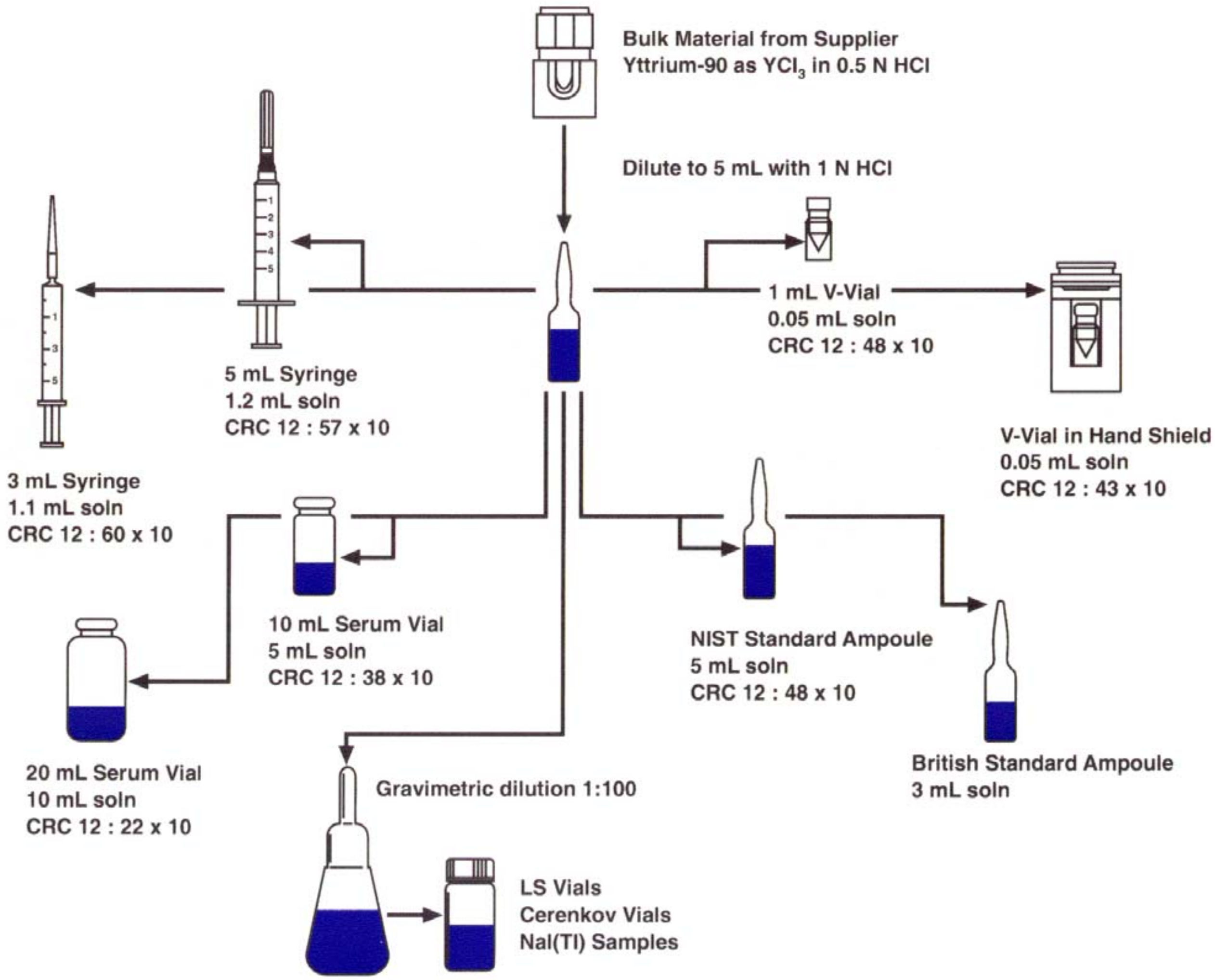


III. Microsphere Assay

	Therasphere®	**SIR-Spheres®**
Vial Geometry	0.3 ml glass v-vial in acrylic shield	5 ml glass vial
Activity	3, 5, 7, 10, 15 or 20 GBq ± 10%	3 GBq ± 10%

- Activity Standard
  - Therasphere activity is traceable to NIST
  - SIR-Sphere activity is not traceable to NIST
    - Apparent activity is 25% greater than indicated
- Transfer standard to local clinic

SOURCE PREPARATION FOR CALIBRATION OF YTTRIUM-90



Y-90 Measurements at NIST

- Liquid scintillation - destructive
  - CIEMAT/NIST
  - Triple-to-Double coincidence method
- Therasphere calibration
  - Calibration for v-vial and v-vial in dose shield in 3 and 20 GBq activities
    - LS of Y90 standard to determine correct dial setting
    - Measure microspheres with dial settings in CRC-12
    - 6 mm change in height = 1% increase in signal

Assay Uncertainty: SIR-Spheres

- Proper Dose Calibrator Setting
  – Reference dose used to determine setting
    - Example: Setting variation was ± 18%
- Additional sources of uncertainty
  – Withdraw administered activity
  – Volume reduction → geometry variation
    - Changes in efficiency for a 0.2 ml sample compared to a 2 ml sample
- Activity in the syringe prior to treatment

Need 1

- Low uncertainty NIST traceable transfer standard for the vendor-specific injection geometry
  - Y90 positron emission calibration
    - Reduces geometry dependence
    - Chamber or source calibration (ADCL)
  - Sr90 calibration
    - Long-lived sample for routine calibration checks

Y90 Positron Emission

- Y90 emits a positron 31.86 ppm
  - Measured using a single high-purity germanium (HPGe) detector
  - More recently measured using a coincidence system (Paxton, UW-Madison)
    - HPGe and NaI
    - High SNR and reduced measurement time
  - 511 keV photon relatively insensitive to geometry differences, unlike beta measurements

Activity Injected

- Microspheres cluster
  - Lodge in 3-way valve, needle, and catheter
  - How much residual activity is trapped?
    - Equipment placed in Capintec
    - Or use radiac to measure dose rate
  - Residual activity in syringe
- Overall Uncertainty > 20%
  - Assumes manufacturer calibration is accurate

Need 2

- NIST traceable post-injection assay of residual activity and trapped activity