

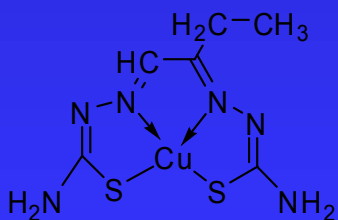
HPLC Validation and Q/A of ^{62}Cu -PTSM, ^{62}Cu -ATSM, and ^{62}Cu -ETS Synthesized by $^{62}\text{Zn}/^{62}\text{Cu}$ Microgenerator Kit

Z. Yue, A. Stephens, and J. L. Lacy
Proportional Technologies, Inc.
Houston, TX

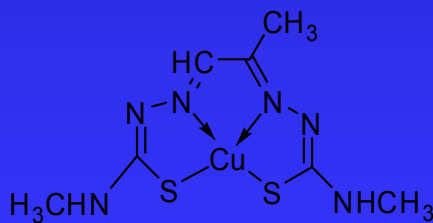


Introduction

- ^{62}Cu labeled bis(thiosemicarbazone) PET agents
 - $^{62}\text{CuPTSM}$
 - $^{62}\text{CuETS}$
 - $^{62}\text{CuATSM}$
- PTI's $^{62}\text{Cu}/^{62}\text{Zn}$ microgenerator with interchangeable instant synthesis kit



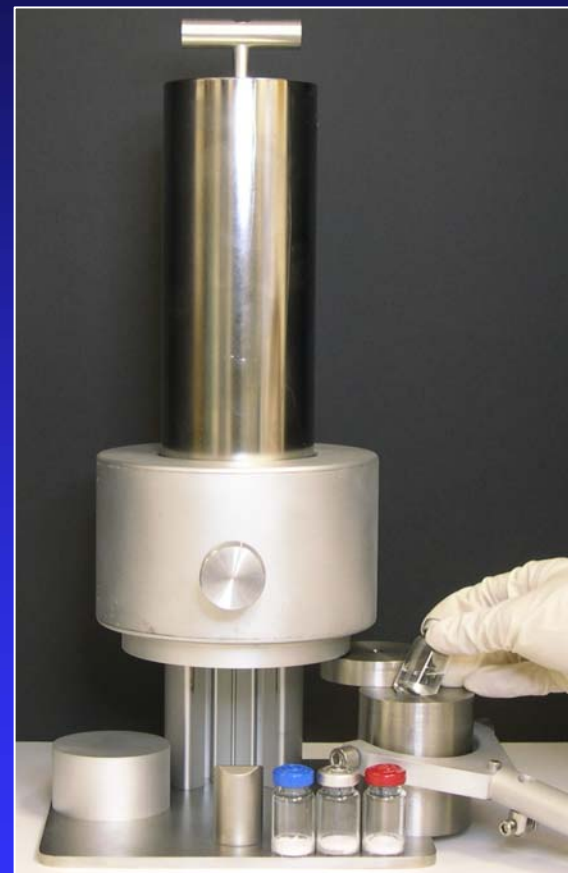
CuETS



CuPTSM



CuATSM

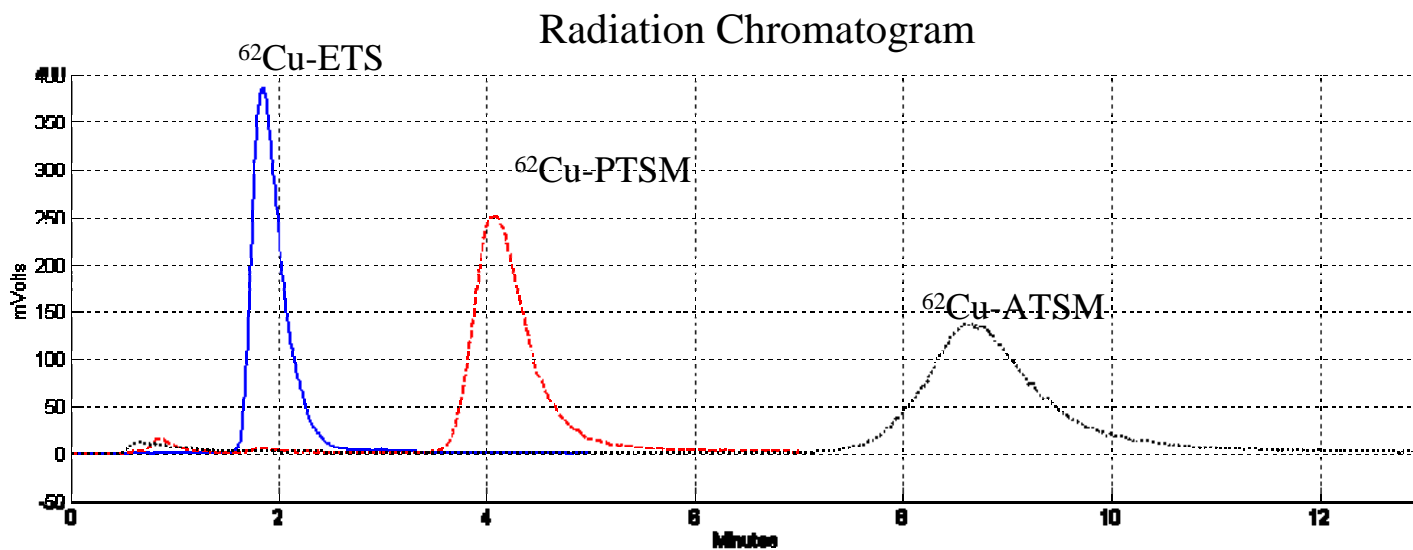
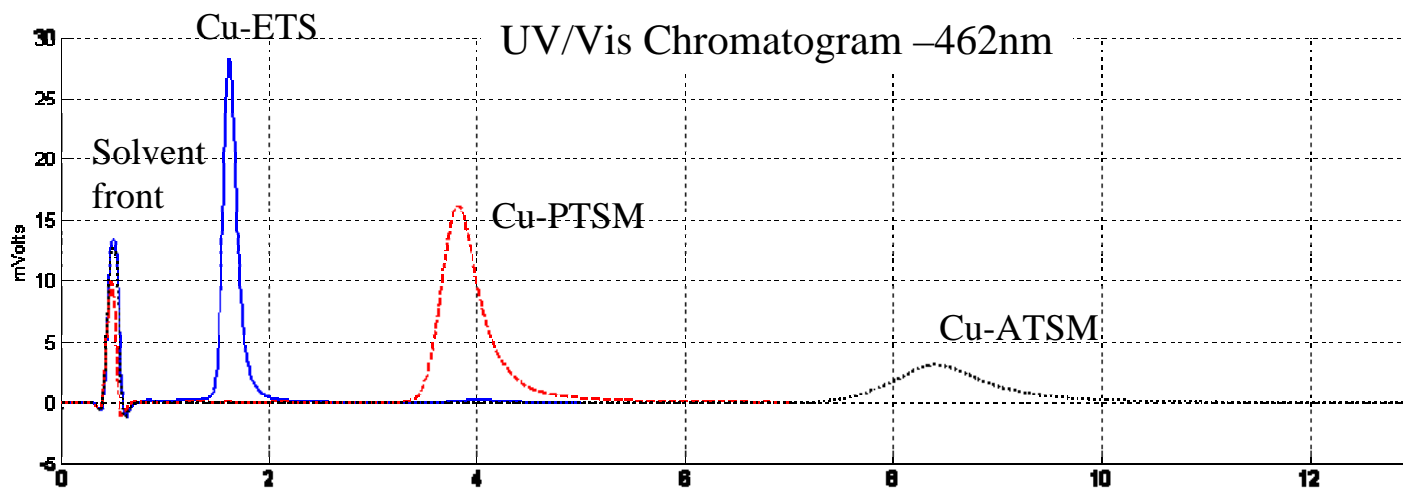


Structure Identity Validation using HPLC

- Media selection
 - Common reverse phase C-18 column
 - Good separation
 - Irreversible binding of Ionic $^{62}\text{Cu}^{2+}$ to column media
 - Reverse phase Oasis[®] HLB column (Waters[™])
 - Good separation
 - Much less binding of Ionic $^{62}\text{Cu}^{2+}$ to column



Structure Identity Validation using HPLC

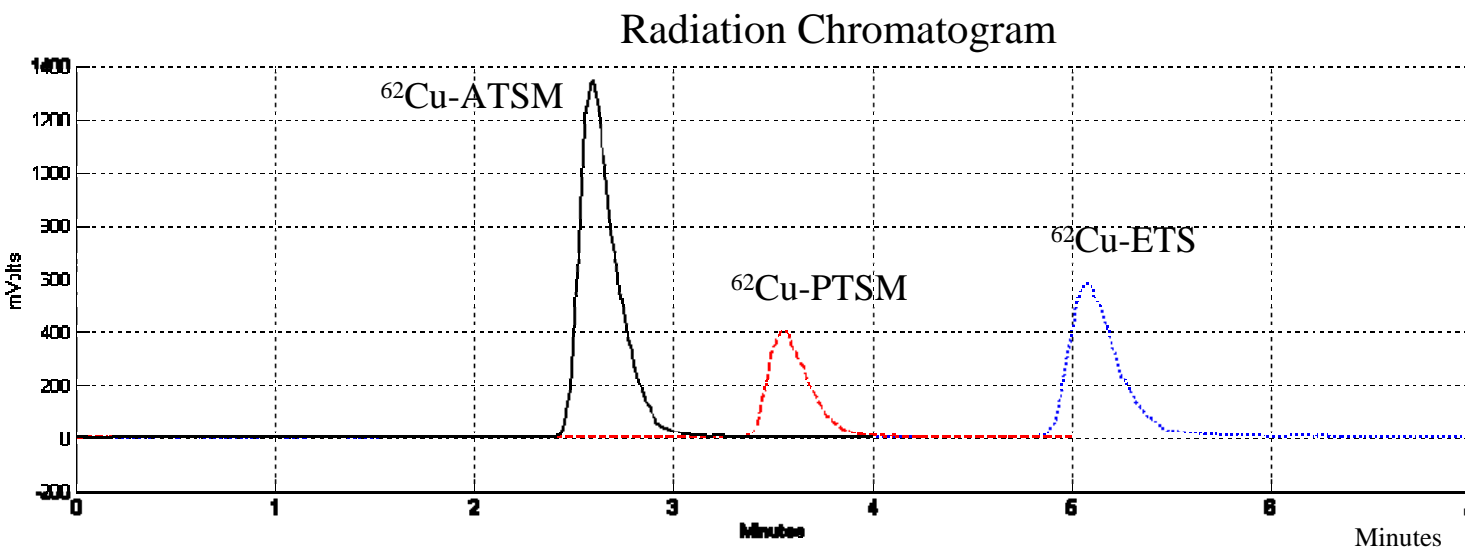
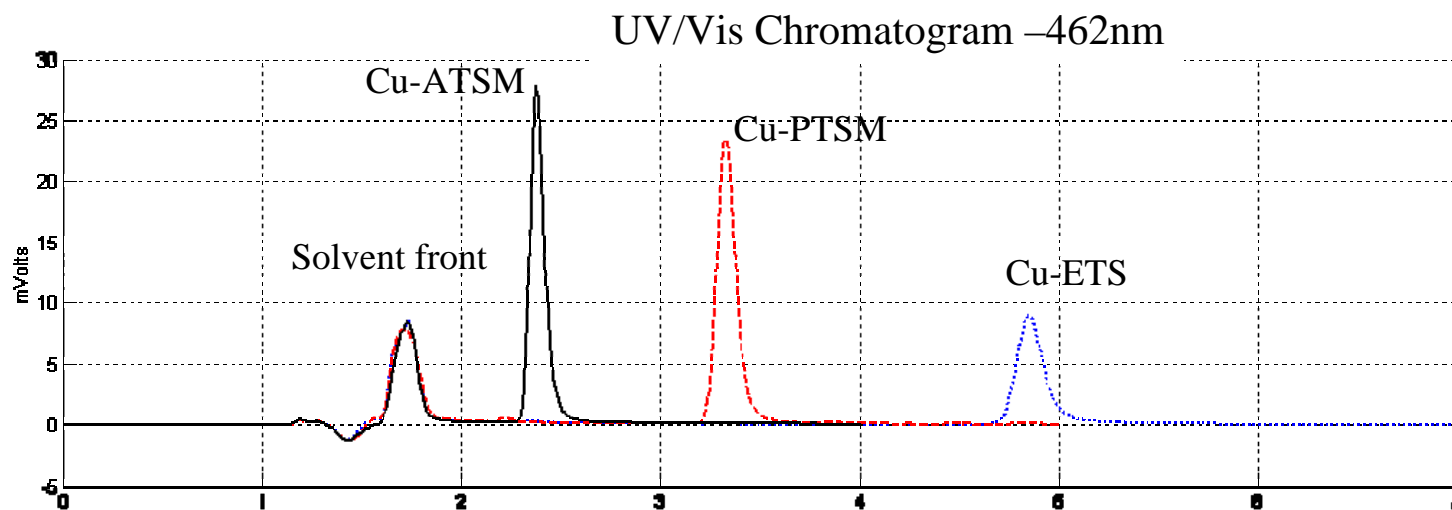


Reverse Phase:
Oasis® HLB
column

HPLC conditions:
Shimadzu Vp system,
with radiation detector,
35% ACN/ 65% 25mM
NaOAc buffer
(pH=4.7), Isocratic
mode (1 mL/min),
40°C,
Amount injected:
Cu-ETS 0.20 µg
Cu-PTSM 0.20 µg
Cu-ATSM 0.20 µg
⁶²Cu-ETS 10.0 µCi
⁶²Cu-PTSM 10.0 µCi
⁶²Cu-ATSM 10.0 µCi

Minutes

Structure Identity Validation using HPLC



Normal Phase:
Nova-Pak[®]
column

Sample Preparation:
Octanol:Hexane
extraction

HPLC conditions:
Shimadzu Vp system,
with radiation detector,
20% EtOH/ 80%
hexane, Isocratic mode
(1 mL/min), 40°C
Amount injected:
Cu-ETS 0.23 μg
Cu-PTSM 0.20 μg
Cu-ATSM 0.20 μg
⁶²Cu-ETS 3.0 μCi
⁶²Cu-PTSM 1.0 μCi
⁶²Cu-ATSM 2.0 μCi

Radiochemical Purity Determination

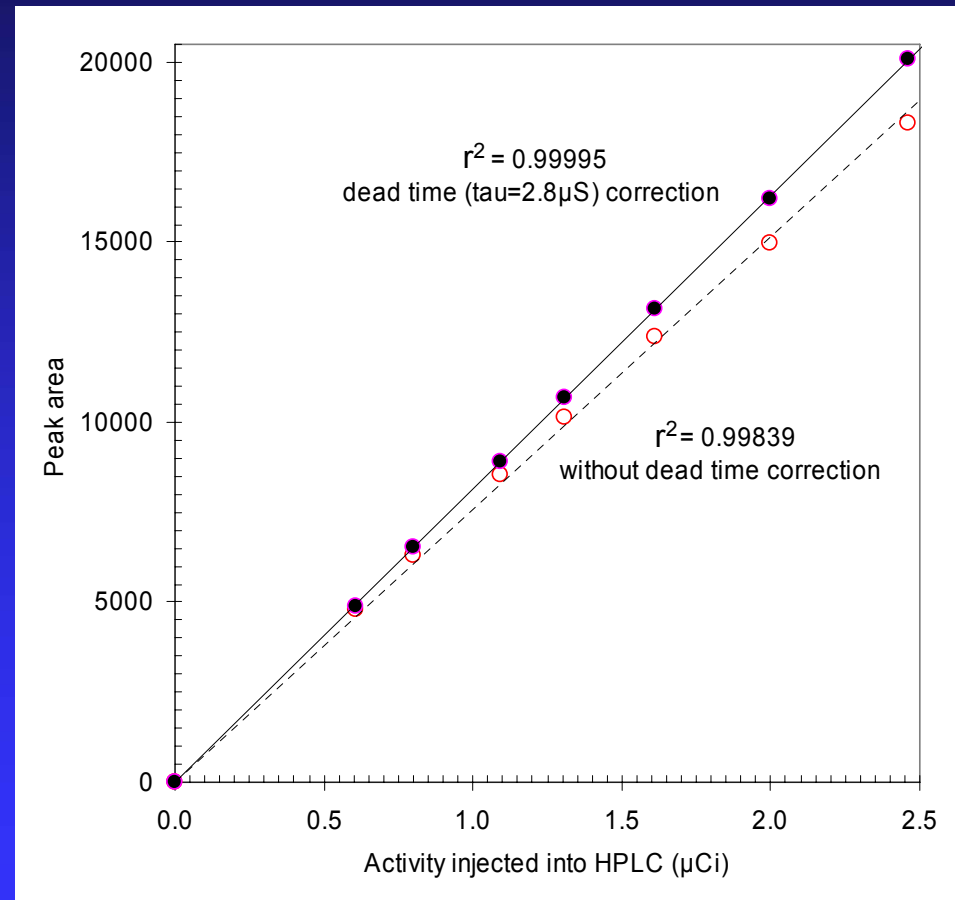
- Activity recovery in HPLC column eluate

	Recovery % (Germanium detector)	Recovery % (Well detector)
$^{62}\text{Cu-ETS}$	101.8 ± 2.3	-
$^{62}\text{Cu-PTSM}$	99.7 ± 1.5	99.2 ± 2.5
$^{62}\text{Cu-ATSM}$	98.8 ± 1.3	101.4 ± 1.0



Radiochemical Purity Determination

- Calibration of Radioflow detector (Berthold) attached with Cerenkov counting cell
 - Dead time correction: paralyzable model
$$m_{\text{observed}} = n_{\text{true}} * \exp(-n_{\text{true}} * t_{\text{au}})$$
 - Better linearity of detector response to dose injected
 - Higher method sensitivity

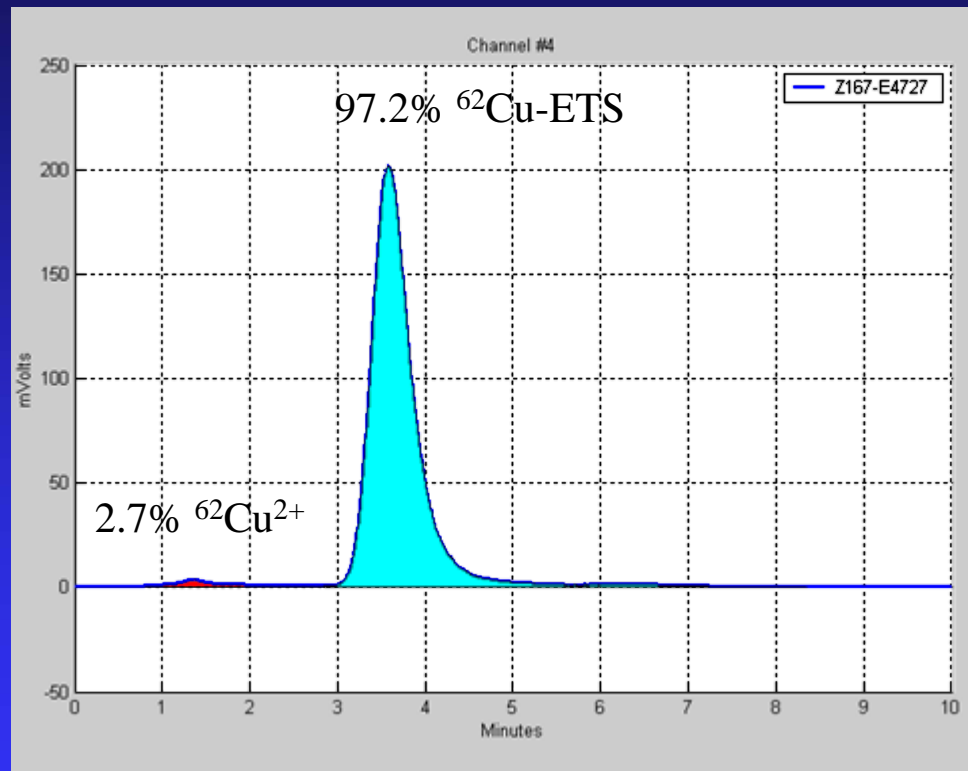


Radiochemical Purity Determination

- Radiochemical purity for ^{62}Cu PET agents produced via PTI instant synthesis Kit is usually measured $>95\%$

Assay Conditions:

Reverse Phase Oasis[®] HLB column
Shimadzu Vp system
Calibrated Radioflow detector
25% ACN/ 75% 25mM NaOAc
buffer for ^{62}Cu -ETS
35% ACN/ 65% 25mM NaOAc
buffer for ^{62}Cu -PTSM
45% ACN/ 55% 25mM NaOAc
buffer for ^{62}Cu -ATSM
Isocratic mode (1 mL/min) at 40°C
 ^{62}Cu injected: $<2.5\text{Ci}$



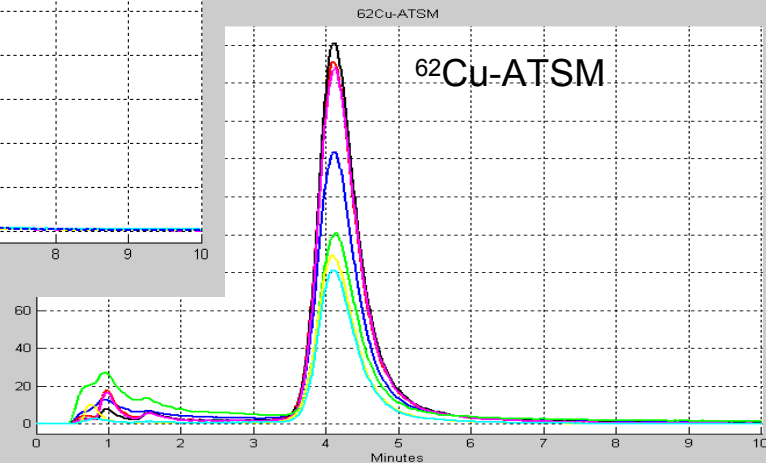
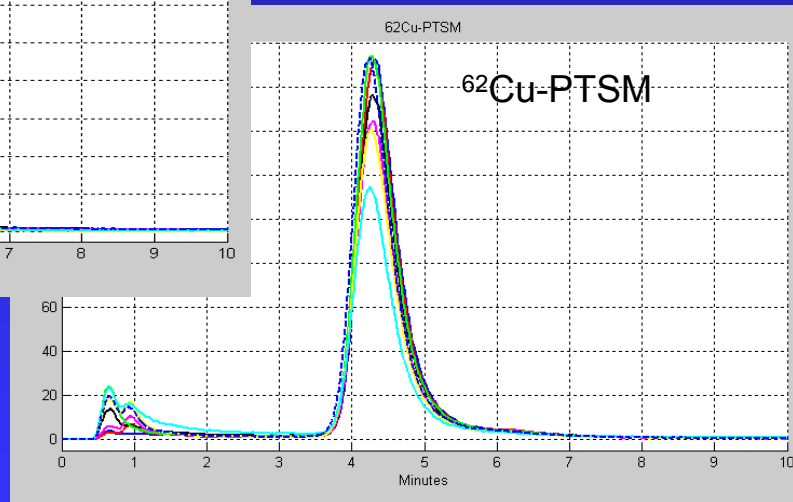
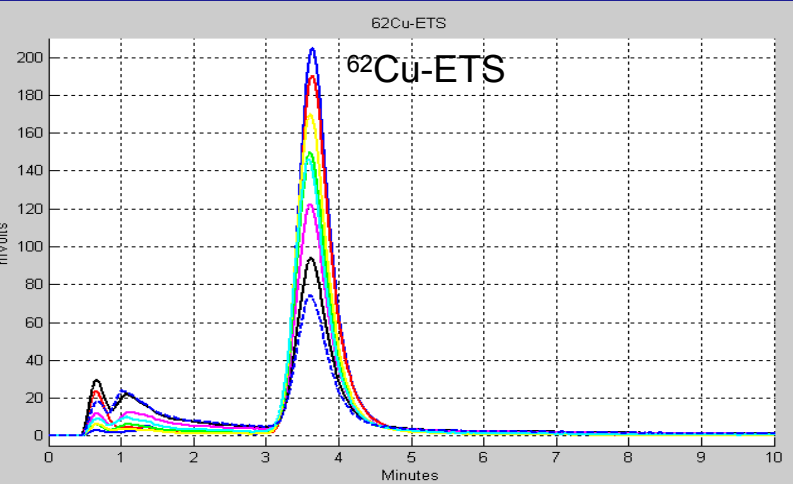
Representative decay corrected radiochromatogram
for micro-generator produced ^{62}Cu -ETS



Radiochemical Purity Determination

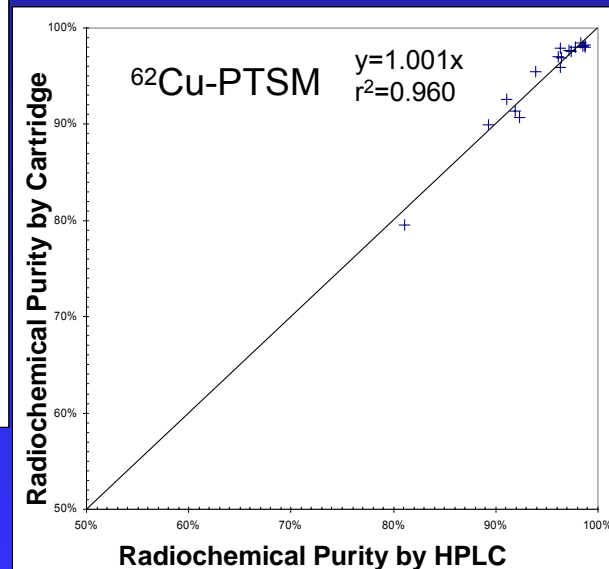
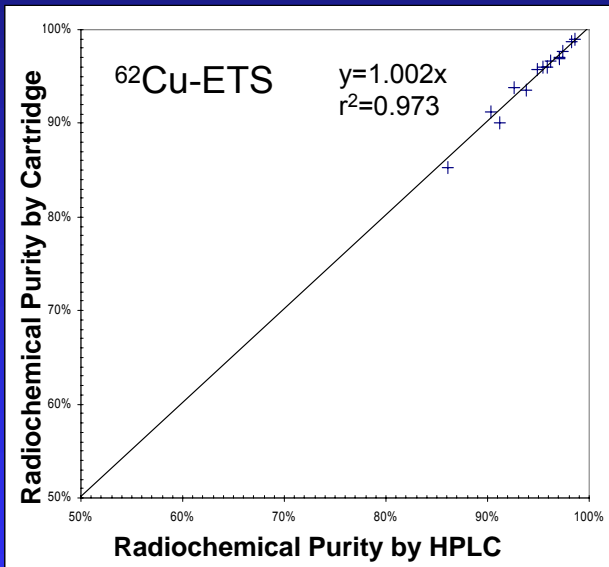
- HPLC performance under extreme circumstances

- Reproducible retention times
- Reliable separation performance

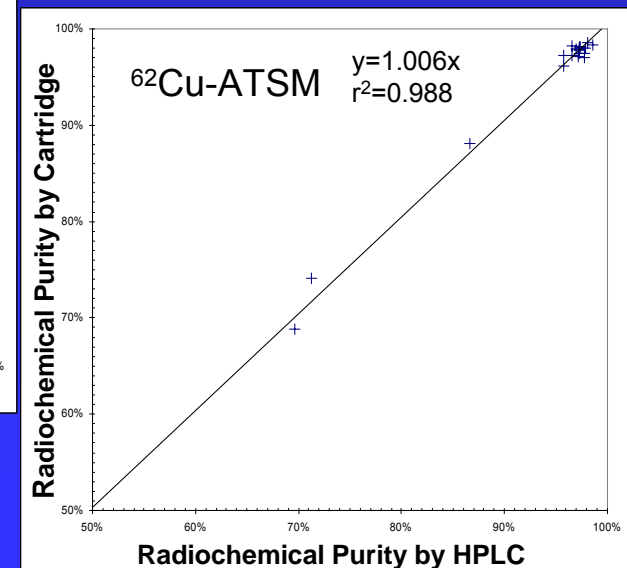


Radiochemical Purity Determination

- Comparison of HPLC and Rapid Cartridge Assay



Oasis® HLB 1cc Extraction Cartridges (Waters™)



Conclusion

- Results from two HPLC separation modes confirm that ^{62}Cu labeled bis(thiosemicarbazone) compounds synthesized via PTI instant synthesis kit have the same molecular structures as the cold references
- HPLC assay of radiochemical purity is accurate and reliable
- Rapid Oasis[®] cartridge assay is competent for Quality Assurance at clinic site

