Theranostic AGuIX Nanoparticles as an MRI Contrast Agent in Patients with Multiple Brain Metastases

J. Stanton-Sheetz[1,2], S. Bennett[3], V.N. Joy[4], N. Jin[5], R. Berbeco[2], and A. Sudhyadhom[2]

1. UMass Lowell, Lowell, Massachusetts, 2. MGB Cancer Institute-Harvard Medical School, Boston, Massachusetts,
3. University of Chicago, Chicago, Illinois, 4. Siemens Healthineers, Erlangen, Germany 5. Siemens Medical Solutions USA, Inc., Malvern, PA

2026 JULY 19–22 VANCOUVER, BC
JOINT AAPM | COMP MEETING

PURPOSE

- AGuIX: **Gadolinium** (Gd) based **nanoparticle** used for **radiosensitization**.
- **Gd** provides **T1 MRI contrast**
- Standard Gadolinium based contrast agents (**GBCA**) are **highly time dependent** where lesion **detectability** is diminished **10 minutes** following injection[1]
- **AGuIX** provides **enhanced tumoral retention**, allowing for imaging up to **3 hours** post infusion.[2]
  - Paired with an MR-Linac, AGuIX could provide **contrast enhancement and radiosensitization for adaptive radiotherapy.**
- **125 lesions** in **Patients** with multiple brain metastases (NCT04899908) were analyzed to assess AGuIX's utility as a contrast agent

METHODS

- **Concentrations** were **calculated** for each GTV using pre- and post- AGuIX MP2RAGE scans.[3]
- Auto-contours were made for **GBCA and AGuIX** MPRAGE scans and were **compared** with **DSC, H_d, $H_{d,95}$, $H_{d,mean}$,** and **contour volume ratios.**
  - Lesions were separated into **small (<0.1 mL)** and **large (≥ 0.1 mL)** to distinguish metric biases based on lesion size
- A voxel-wise comparison was also done to **separate lesions** based on **uptake distribution differences**

CONTACT

Justin Stanton-Sheetz
UMass Lowell – MGB Cancer Institute
jsheetz1@bwh.Harvard.edu

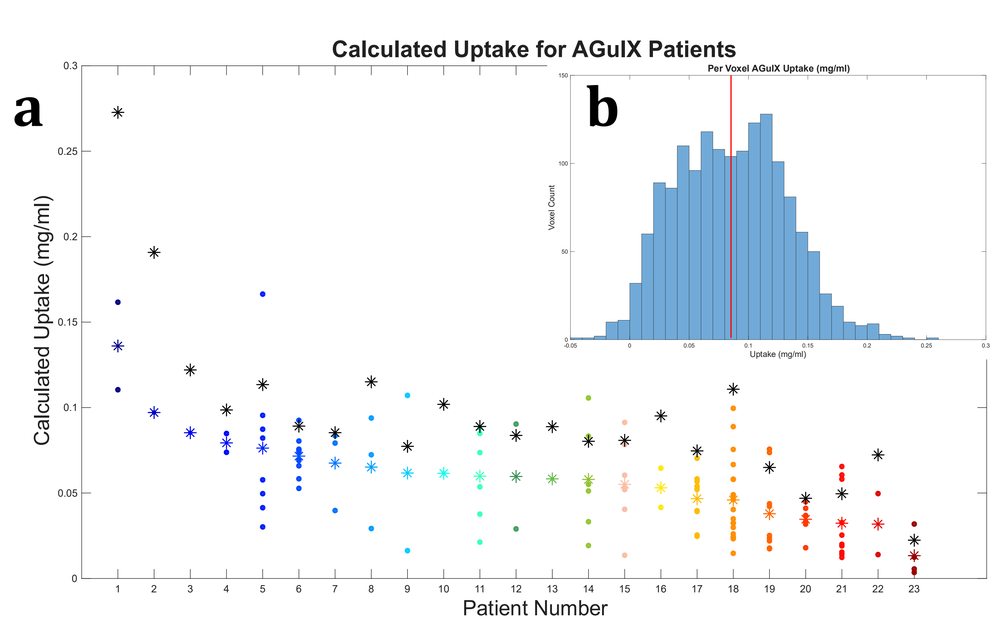

Figure 1: a Calculated mean uptake per patient sorted by descending mean concentration per patient. 125 total lesions were included. Dots indicate average uptake within a single lesion. Colored asterisks indicate mean uptake within all the lesions in a patient. Black asterisks indicate the mean upper quartile uptake per patient. Average uptake was 0.0604 mg/mL with a range of 0.00354–0.162 mg/mL. b Uptake histogram for an example lesion indicating how average uptake was calculated on a per lesion basis

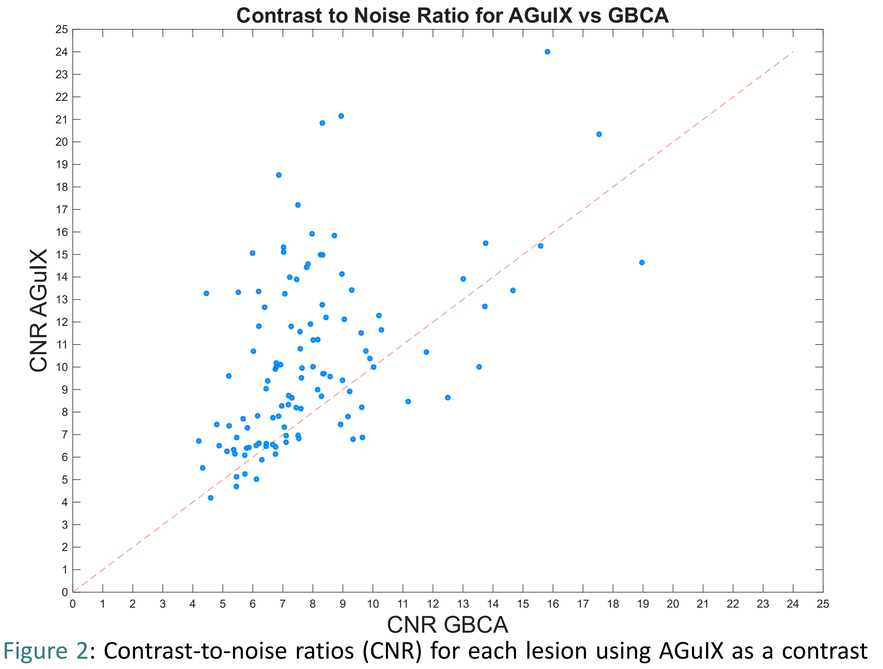

Figure 2: Contrast-to-noise ratios (CNR) for each lesion using AGuIX as a contrast agent vs standard GBCA for contrast. The dotted red line indicates a slope of 1. Most points lie above this line indicating CNR was typically higher for AGuIX than for GBCA. This is possibly influenced by a more homogenous contrast distribution throughout the lesion seen in AGuIX **whereas GBCA tended to uptake more on the edge of the lesion**

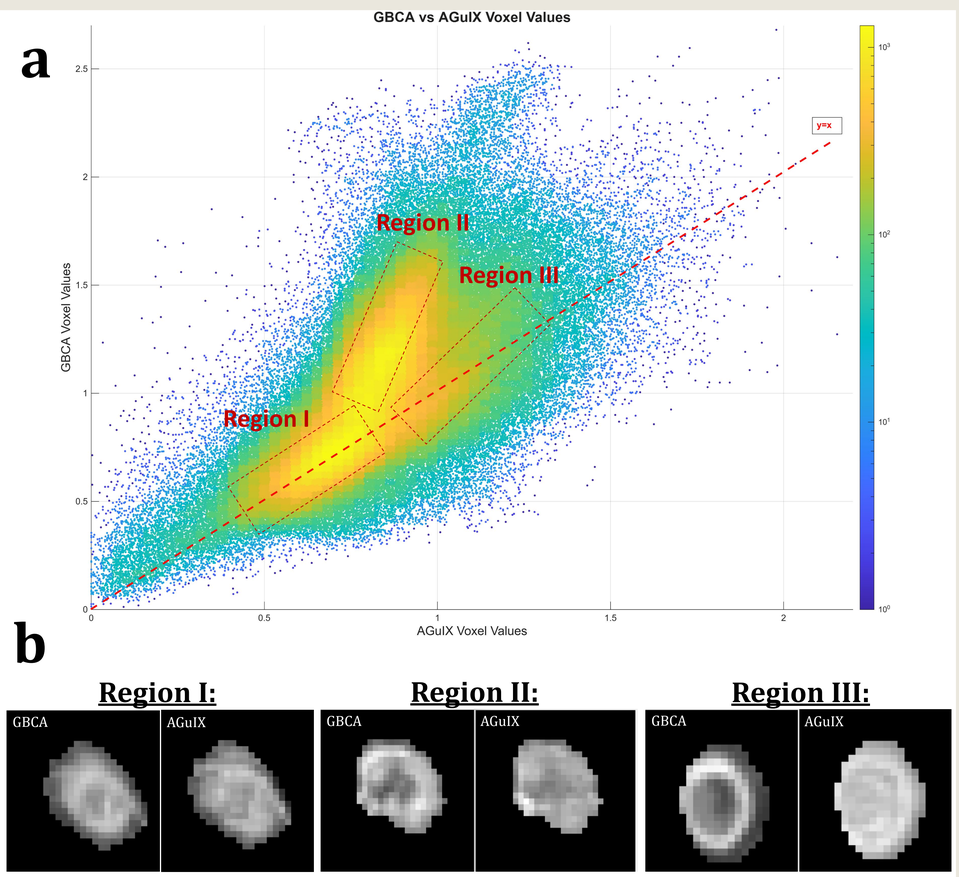

Figure 3: a Voxel-value to voxel-value comparison for GBCA MPRAGE scans vs AGuIX MPRAGE scans following bias correction and normalization within physician drawn contours for all lesions. A heat map is applied showing point density. Regions are annotated where patterns appear to emerge in voxel-value comparison, indicating uptake distribution differences or similarities. b Examples of lesions separated by region, chosen by voxel-value density. Region I grouped lesions with more homogenous uptake. Region II contains lesions with similar uptake distribution between GBCA and AGuIX. Region III includes the most prominent uptake distribution differences.

	DSC	H_d (mm)	$H_{d,95}$ (mm)	$H_{d,\mathrm{mean}}$ (mm)	Volume Ratio (GBCA:AGuIX)
GTV < 0.1 mL	0.81 ± 0.19	1.14 ± 0.42	0.98 ± 0.43	0.18 ± 0.17	1.18 ± 0.83
GTV >= 0.1 mL	0.87 ± 0.13	2.07 ± 1.91	1.32 ± 1.15	0.36 ± 0.46	1.08 ± 1.41
p-value	0.12	p < 0.001	0.031	p < 0.001	0.056
Overall	0.86 ± 0.14	1.92 ± 1.80	1.27 ± 1.08	0.34 ± 0.44	1.10 ± 1.33

Table 1: DSC, H_d, $H_{d,95}$, $H_{d,\mathrm{mean}}$, and contour volume ratios for GBCA auto-contours compared to AGuIX auto-contours, separated by small (<0.1 mL) and large (≥ 0.1 mL) lesions. Values are reported as mean ± standard deviation. . Lesion group distributions were tested with a Kruskal-Wallace test and p-values for H_d and $H_{d,\mathrm{mean}}$ indicate statistical significance.

DISCUSSION

- AGuIX uptake had a large range within and across patients. Individual lesion uptake may influence nanoparticle distribution and contour performance.
  - Nanoparticle pharmacokinetics require further investigation to understand the influence of physiological characteristics on nanoparticle uptake.
- AGuIX contour performance shows it can reliably delineate GTV margins for most lesions.
- AGuIX typically exhibited a more uniform uptake distribution within the lesion. More research is required to understand the impact on RT planning.

Conclusions

AGuIX is shown to be a reliable contrast agent for GTV delineation. Uptake distribution differences and enhanced retention have potential to differentiate physiological characteristics in lesions

References

1. Jeon JY, Choi JW, Roh HG, Moon WJ. Effect of Imaging Time in the Magnetic Resonance Detection of Intracerebral Metastases Using Single Dose Gadobutrol. Korean J Radiol 2014; 15: 145.
2. Lux F, Tran VL, Thomas E, et al. AGuIX® from bench to bedside-Transfer of an ultrasmall theranostic gadolinium-based nanoparticle to clinical medicine. Br J Radiol 2019; 92. DOI:10.1259/BJR.20180365.
3. Bennett S, Verry C, Kaza E, et al. Quantifying gadolinium-based nanoparticle uptake distributions in brain metastases via magnetic resonance imaging. Sci Rep 2024; 14: 1–11.