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**Full Reference**:

**Abstract 1**

**Title**: Evaluation of [$^{68}$Ga]Ga-PSMA-617 PET as a diagnostic agent in recurrent glioblastoma patients: results of the Genesis GBM 001 phase I/II study.

**Authors**: **C. Brighi**[1], S. Puttick[2], David Waddington[1], Paul Keall[1], Vicki Sproull[3], Paul Tooney[4], Michael Fay[3,4]

**Affiliations**: 1. Image X Institute, Sydney School of Health Sciences, Faculty of Medicine and Health, The University of Sydney, Sydney, Australia 2. AdvanCell Isotopes Pty Ltd, Sydney, Australia 3. GenesisCare, Newcastle, Australia 4. MHF Centre for Brain Cancer Research, College of Health, Medicine and Wellbeing, University of Newcastle, Newcastle,Australia.

**Abstract 2**

**Title**: Preliminary findings from the MRI quality assurance programme for the prospective multi-site Australian FIG ([18F]-FET-PET in Glioblastoma) TROG 18.06 study.

**Authors**: **C. Brighi**[1], B.A. Moffat[2], A. Whitehead[3], O. Cook[3], A. Moore[3], A. Grose[3], A. Rossi[3], R. Dykyj[3], E. Lau[2,4], G. Fitt[2,4], A. Lasocki[5], H.K. Gan[6,7], A.M. Scott[2,4,6,7], E-S. Koh[8,9]

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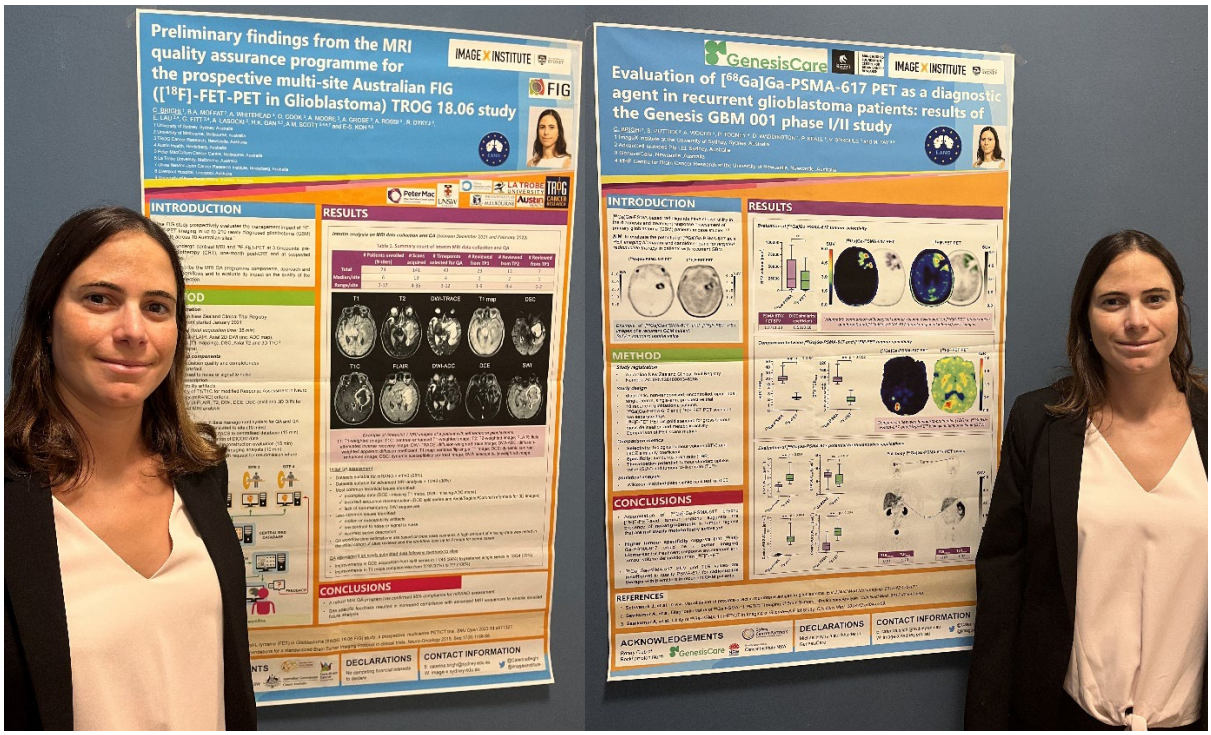
**Conference/Meeting Name**: 18$^{th}$ Meeting of the European Association of Neuro-Oncology (EANO 2023)
**Location** (city, state, country): Rotterdam, The Netherlands
**Dates**: 21-24 September 2023
**Presentation Type**: Posters




The European Association in Neuro-Oncology (EANO) Annual Meeting is the second largest neuro-oncology conference in the world. This year, over 1000 researchers and clinicians attended from 50 different countries. During the congress, speakers from across the globe presented the latest clinical trial outcomes and highlighted key advances in basic and translational science in neuro-oncology. The key clinical themes of the Rotterdam 2023 meeting included experimental and combination therapies, the latest on radiation oncology technologies, neurosurgical precision tools, advanced imaging modalities and the latest developments in molecular diagnostics.

The use of low-intensity focused ultrasound to enhance chemotherapeutics delivery across the blood-brain barrier in brain cancer patients was an area that received a lot of attention.

Attending this conference consolidated my research idea that using multimodal imaging to guide more precise and effective surgical and radiation treatments is an area of interest for clinicians in neuro-oncology. I finally had the opportunity to meet in person a team of neurosurgeons from the Amsterdam University Medical Centre, whom I have been collaborating with for the past two years. Our meeting was instrumental to discuss new ideas for a collaboration research study and for a joint grant application. My collaborators also introduced me to the Head of Radiation Oncology at the Amsterdam University Medical Centre, who expressed his interest in supporting our research study proposal. Finally, during the conference I also met a neuro-radiologist from UCLA, who seemed very interested in my research work and expressed interest in discussing a future collaboration.

The new knowledge of the current challenges faced by clinicians managing brain cancer patients gave me confidence that my research ideas are relevant to the field and would have an impactful clinical application. Strengthening my international collaboration network will also help me grow international recognition in the field of neuro-oncology and will increase my chance of successful and impactful research outcomes.

Using multimodal imaging to help clinical decision-making and guide more precise and more effective treatments can certainly lead to better clinical practice in the management of all types of cancer. This approach will give clinicians important tools to make more confident treatment decisions and will improve patients quality of life by reducing toxicity to healthy functional tissue with more focused treatments.

Overall, I really enjoyed the multidisciplinary aspect of the EANO conference. As a scientist in brain cancer imaging, understanding what are the clinical challenges in the field of neuro-oncology and meeting experts from different disciplines is the best way to generate new research ideas and evaluate the impact they could have on clinical translation.

# Evaluation of [$^{68}$Ga]Ga-PSMA-617 PET as a diagnostic agent in recurrent glioblastoma patients: results of the Genesis GBM 001 phase I/II study

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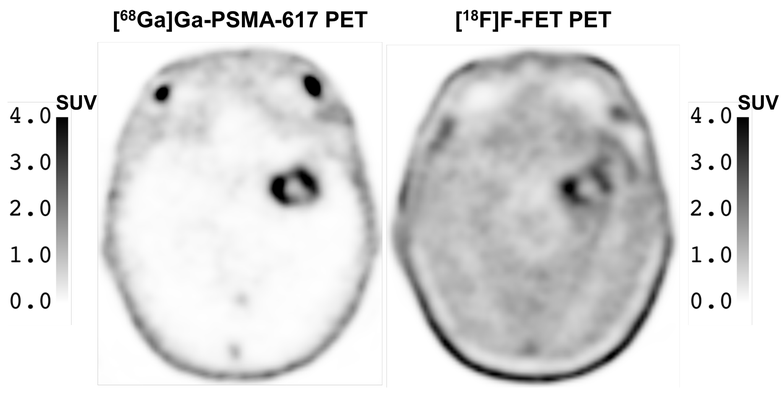
## INTRODUCTION

[$^{68}$Ga]Ga-PSMA-based radioligands have shown utility in the diagnosis and treatment response assessment of primary glioblastoma (GBM) patients in case studies.[1-3]

**AIM**: to evaluate the potential of [$^{68}$Ga]Ga-PSMA-617 as a PET *imaging biomarker* and candidate ligand for *targeted radionuclide therapy* in patients with recurrent GBM.




*Example of [$^{68}$Ga]Ga-PSMA-617 and [$^{18}$F]F-FET PET images of a recurrent GBM patient.*
*SUV = standard uptake value*

## METHOD

***Study registration***

- Australian New Zealand Clinical Trial Registry
- Number: ACTRN12618001346268

***Study design***

- diagnostic, non-randomised, uncontrolled, open-label, single-centre, single-arm, prospective trial
- **10** recurrent glioblastoma patients
- [$^{68}$Ga]Ga-PSMA-617 and [$^{18}$F]F-FET PET scans on two separate days
- [$^{18}$F]F-FET PET as gold standard for gross tumour mass delineation and metabolic activity
- Comparison of PET scans metrics

***Comparison metrics***

- **Selectivity**: biological tumour volume (BTV) and DICE similarity coefficient
- **Specificity**: tumour-to-brain ratio (TBR)
- **Theranostics potential**: tumour standard uptake value (SUV) and tumour-to-liver ratio (TLR)

***Statistical analysis***

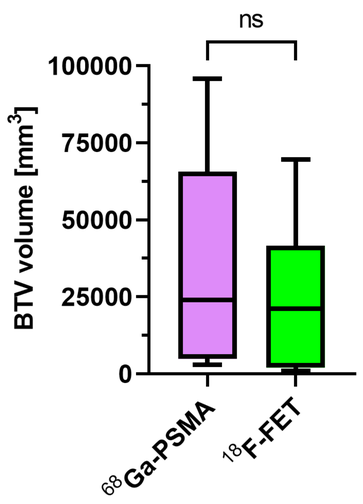
- Wilcoxon matched-pairs signed rank test, α=0.05

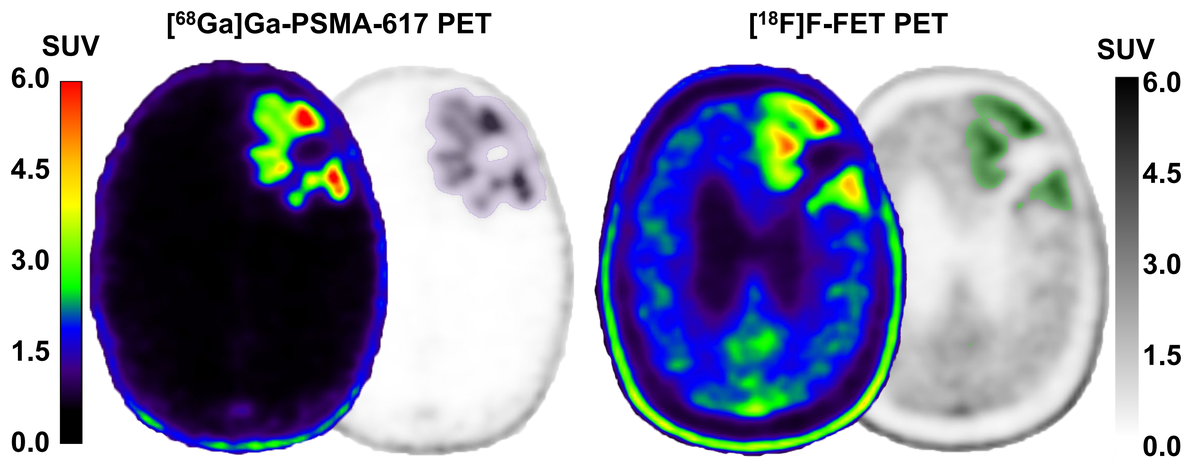
## CONCLUSIONS

- Accumulation of [$^{68}$Ga]-Ga-PSMA-617 beyond [$^{18}$F]F-FET-avid tumour regions suggests the presence of **neoangiogenesis** in tumour regions that are **not overly metabolically active** yet.
- **Higher tumour specificity** suggests that [$^{68}$Ga]-Ga-PSMA-617 could be a **better imaging biomarker** for treatment response assessment and tumour volume delineation than [$^{18}$F]F-FET.
- [$^{68}$Ga]-Ga-PSMA-617 SUV and TLR values are **insufficient** to qualify PSMA-617 for **radionuclide therapy** with β-emitters in recurrent GBM patients.

## RESULTS

***Evaluation of [$^{68}$Ga]Ga-PSMA-617 tumour selectivity***

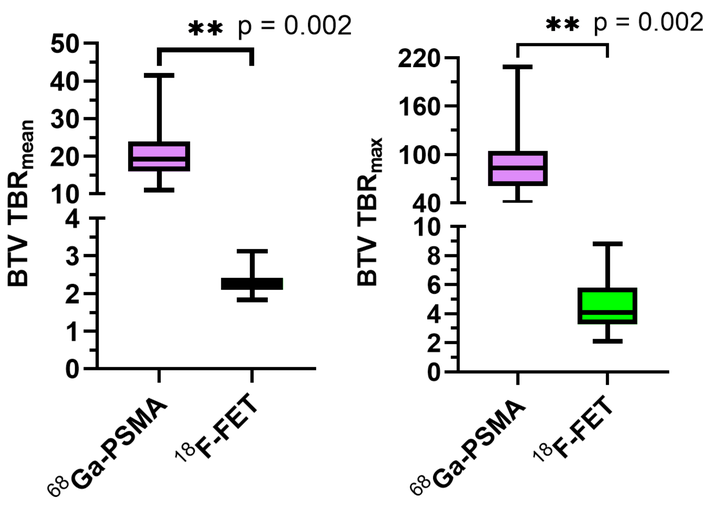


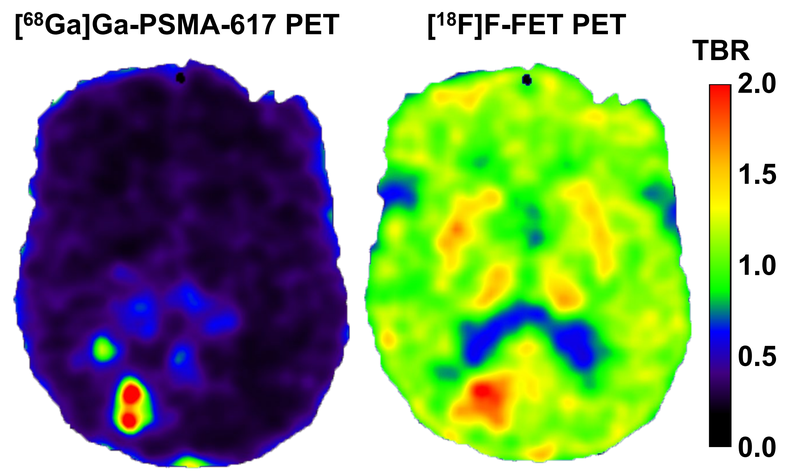




| PSMA BTV/ FET BTV | DICE similarity coefficient |
|---|---|
| 1.87±1.10 | 0.58±0.18 |

*Volumetric comparison of biological tumour volume delineated on [$^{18}$F]F-FET (green region of interest) and [$^{68}$Ga]Ga-PSMA-617 (purple region of interest) PET images.*

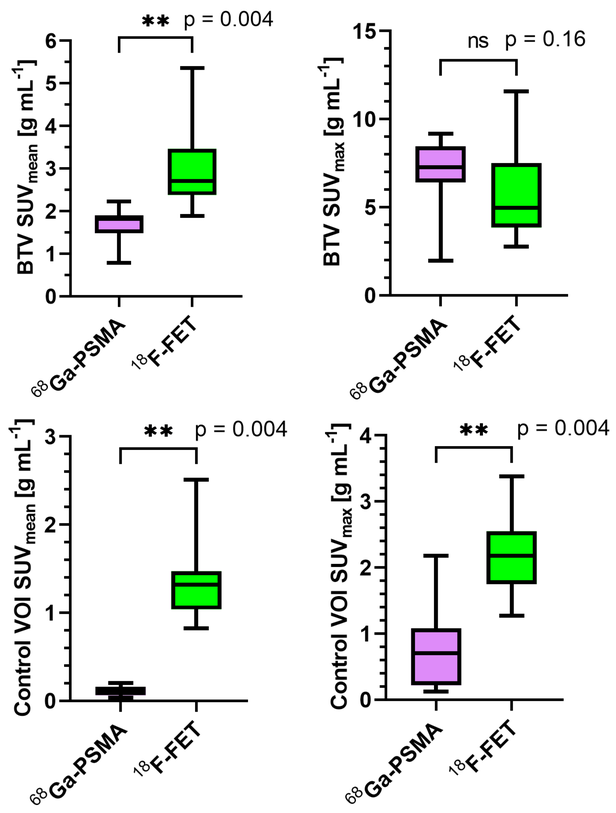
***Comparison between [$^{68}$Ga]Ga-PSMA-617 and [$^{18}$F]F-FET tumour specificity***

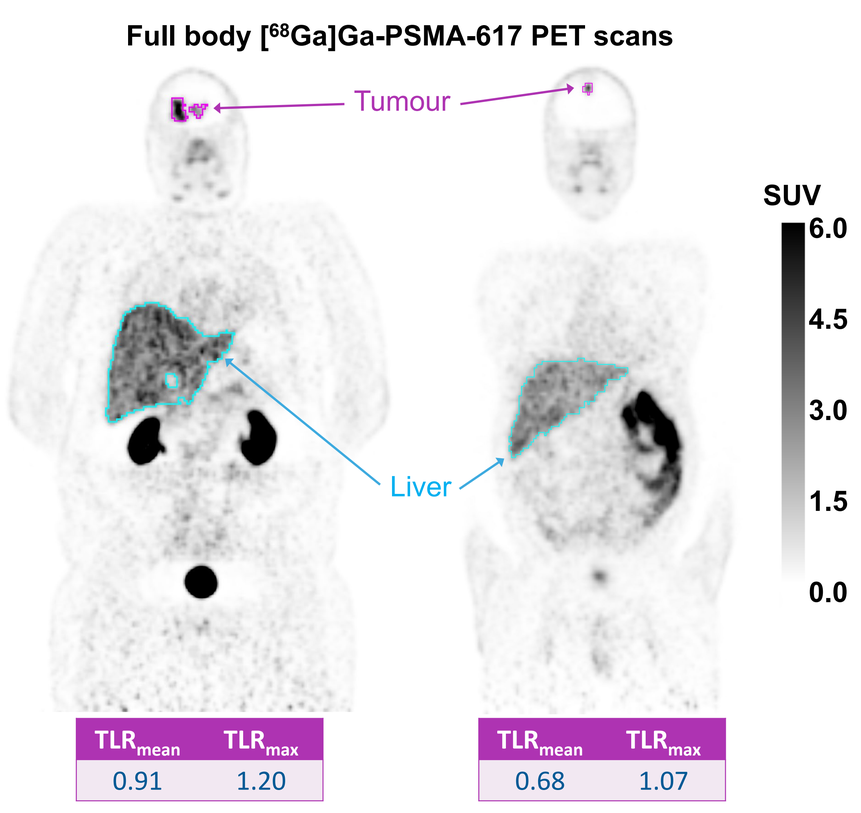



*Comparison between tumour-to-brain ratio (TBR) in [$^{68}$Ga]Ga-PSMA-617 and [$^{18}$F]F-FET biological tumour volume (BTV).*

***Evaluation of [$^{68}$Ga]Ga-PSMA-617 potential for theranostics applications***




| $TLR_{mean}$ | $TLR_{max}$ |
|---|---|
| 0.91 | 1.20 |

| $TLR_{mean}$ | $TLR_{max}$ |
|---|---|
| 0.68 | 1.07 |

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3. **Sasikumar A, et al**. Utility of $^{68}$Ga-PSMA-11 PET/CT in Imaging of Glioma—A Pilot Study. *Clin Nucl Med. 2018;43:e304-e309*.

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## DECLARATIONS

Michael Fay is a stockholder in GenesisCare

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# Preliminary findings from the MRI quality assurance programme for the prospective multi-site Australian FIG ([$^{18}$F]-FET-PET in Glioblastoma) TROG 18.06 study

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## INTRODUCTION

The FIG study prospectively evaluates the management impact of $^{18}$F-FET-PET imaging in up to 210 newly diagnosed glioblastoma (GBM) patients across 10 Australian sites.[1]

Patients undergo contrast MRI and $^{18}$F-FET-PET at 3 timepoints: pre-chemoradiotherapy (CRT), one-month post-CRT and at suspected progression.

**AIM**: to describe the MRI QA programme components, approach and integrated workflows and to evaluate its impact on the quality of the MRI data collection.

## METHOD

***Study registration***

- Australian New Zealand Clinical Trial Registry
- Recruitment started January 2021

***MRI protocol*** *(total acquisition time: 35 min)*

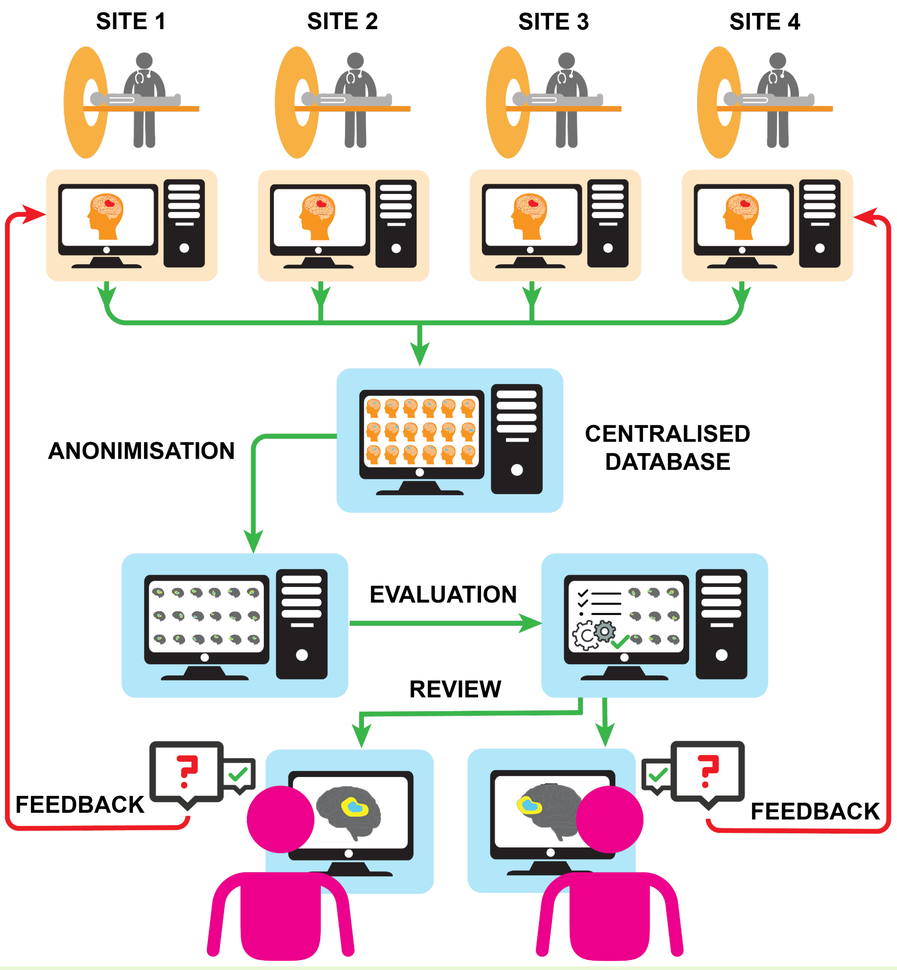
- 3D-T1, 3D-FLAIR, Axial 2D DWI (inc. ADC map), DCE (inc. T1 mapping), DSC, Axial T2 and 3D T1C [2]
- SWI optional

***QA assessed components***

- data acquisition quality and completeness
- motion artefact
- low contrast to noise or signal to noise
- series description
- susceptibility artifacts
- suitability of T1/T1C for modified Response Assessment in Neuro Oncology (mRANO) criteria
- suitability of FLAIR, T2, DWI, DCE, DSC (SWI and 3D DIR) for advanced MRI analysis

***QA workflow***

1. Participant setup in data management system for QA and QA requirements communicated to site (10 mins)
2. site upload from local PACS to centralised database (15 min)
3. automated anonymisation of DICOM data
4. data completeness and reconstruction evaluation (15 min)
5. review by two expert neuroimaging analysts (10 min)
6. sites received feedback with request for resubmission where required (5 min)



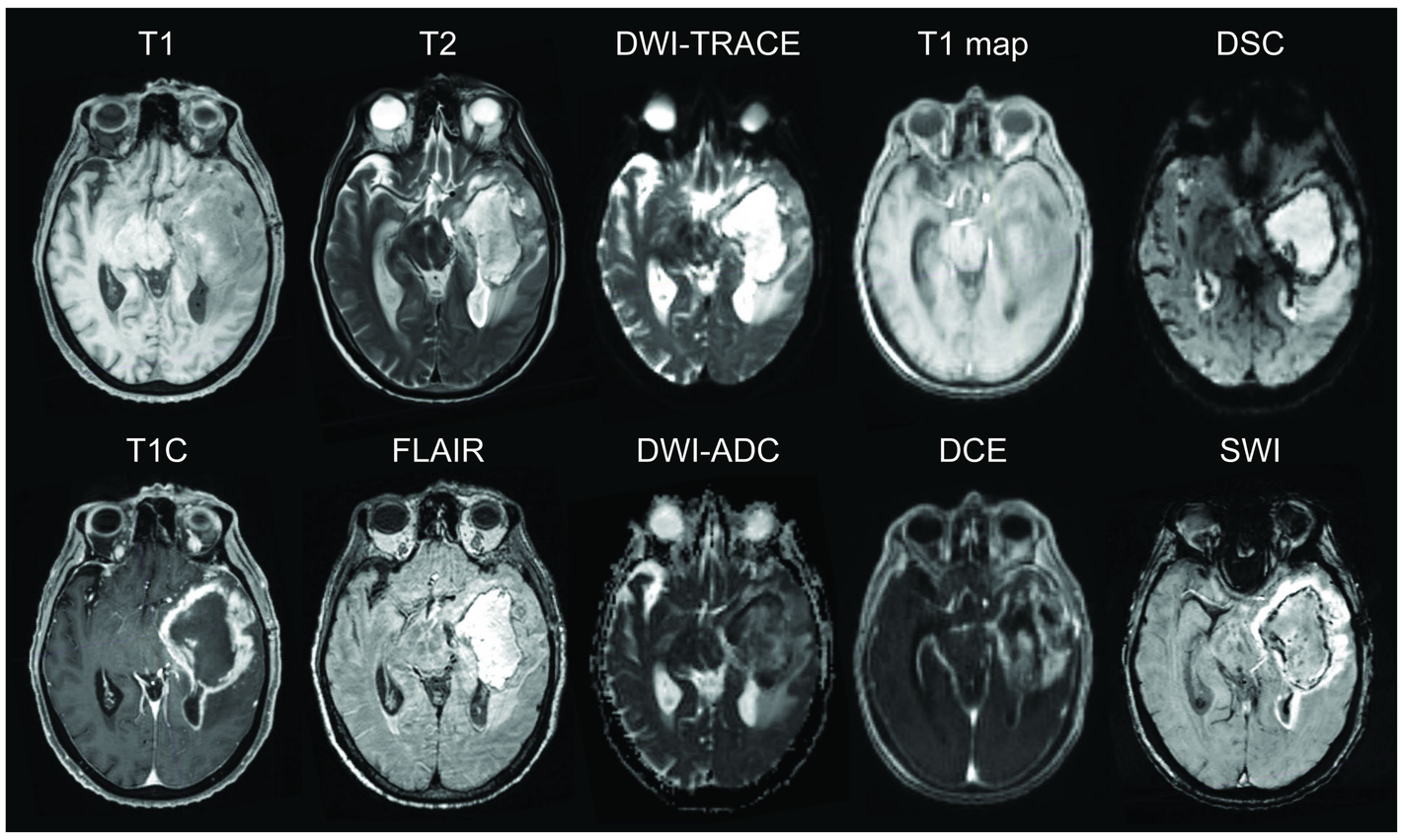

*Scheme of MRI QA workflow.*

## RESULTS

***Interim analysis on MRI data collection and QA*** *(between December 2021 and February 2023)*

**Table 1. Summary count of interim MRI data collection and QA**

| | # Patients enrolled (9 sites) | # Scans acquired | # Timepoints selected for QA | # Reviewed from TP1 | # Reviewed from TP2 | # Reviewed from TP3 |
|---|---|---|---|---|---|---|
| Total | 74 | 141 | 43 | 23 | 13 | 7 |
| Median/site | 6 | 13 | 4 | 2 | 2 | 1 |
| Range/site | 2-17 | 4-35 | 3-12 | 1-6 | 0-4 | 0-2 |




*Example of timepoint 1 MRI images of a patient with left temporal glioblastoma.*
T1: T1-weighted image; T1C: contrast enhanced T1-weighted image; T2: T2-weighted image; FLAIR: fluid attenuated inverse recovery image; DWI-TRACE: diffusion-weighted trace image; DWI-ADC: diffusion-weighted apparent diffusion coefficient; T1 map: variable flip angle T1 image; DCE: dynamic contrast enhanced image; DSC: dynamic susceptibility contrast image; SWI: susceptibility-weighted image.

Initial QA assessment

- Datasets suitable for mRANO = 41/43 (95%)
- Datasets suitable for advanced MRI analysis = 13/43 (30%)
- Most common technical issues identified:
  - ✓ incomplete data (DCE - missing T1 maps, DWI - missing ADC maps)
  - ✓ incorrect sequence reconstruction (DCE split series and Axial/Sagittal/Coronal reformats for 3D images)
  - ✓ lack of non-mandatory SWI sequences
- Less common issues identified:
  - ✓ motion or susceptibility artifacts
  - ✓ low contrast to noise or signal to noise
  - ✓ incorrect series description
- QA workflow time estimations are based on best case scenario. A high amount of missing data was noted in the initial cohort of case reviews and the workflow took up to 3 hours for some cases

QA assessment on newly submitted data following feedback to sites

- improvements in DCE acquisition from split series in 11/45 (24%) to preferred single series in 18/24 (75%)
- Improvements in T1 maps completeness from 7/19 (37%) to 7/7 (100%)

## CONCLUSIONS

- A robust MRI QA program has confirmed 95% compliance for mRANO assessment
- Site specific feedback resulted in increased compliance with advanced MRI sequences to enable detailed future analysis

## REFERENCES

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2. **Ellingson et al**. Consensus recommendations for a standardized Brain Tumor Imaging Protocol in clinical trials. *Neuro-Oncology* 2015; Sep;17(9):1188-98.

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## DECLARATIONS

No competing financial interests to declare

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