High throughput MRI in the use and development of preclinical mouse tumor models

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MOTIVATION

1. Determination of anticancer activity in mice relies on high throughput methodology
2. Rapid development of new transgenic cancer models is also facilitated by high-throughput screening.
3. While MRI has unique advantages in the above applications, the potential of in vivo MRI has been throughput-limited.
4. Complex new approaches that may enable parallel MRI of multiple mice, are in the early stages of development and will not be widely available in the short term at an affordable level.

AIMS

1. To provide a benchmark for future MRI throughput improvements with parallel strategies.
2. To demonstrate the mouse imaging throughput that is currently attainable with standard high field MRI hardware available today.
3. To determine the feasibility of using high-throughput diffusion MRI to monitor efficacy in preclinical drug trials.
4. To determine the feasibility of high-throughput MRI determination of tumor appearance and development in a tv-a transgenic mouse model of glioma

PRECLINICAL MODELS	METHODS	THROUGHPUT OPTIMIZATION	MRI PULSE SEQUENCE DESIGN	MRI DATA AND RESULTS	MOUSE THROUGHPUT (average time per mouse including preparation and MRI, over entire study duration)

SC HUMAN TUMOR XENOGRAFT MOUSE MODEL

- PANC-1 tumor implanted subcutaneously.
- Treatment group (n=5) received 160mg/kg Gemsar on Days 0, 3, 7, 10.
- Diffusion MRI every 3-4 days over 1 month.
- Tumor volume and apparent diffusion coefficient (ADC) quanitifed

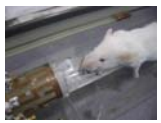
(see poster abstract # 5116)

TV-A TRANSGENIC MOUSE MODEL OF GLIOMA

- PDGF-driven glioma in transgenic nestin tv-a mice [2] **(see poster abstract # 5115)**
- At birth, mice received an intracranial injection of cells infected with RCAS virus expressing PDGF
- Weekly MRI from 3 weeks age to determine tumor appearance and development over a period of 16 weeks.

MRI RF COILS

- State of the art quadrature RF volume coils based on the birdcage design
- Rapid and robust tuning and matching
- High signal-to-noise and homogeneity



ANIMAL POSITIONING

- 'Sled' for rapid and reproducible mouse positioning
- 'Bite bar' for reproducible positioning of animal on sled

ANIMAL IMMOBILIZATION

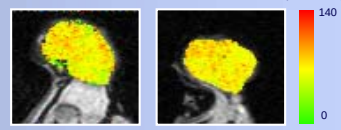
- Detachable straps to restrict motion in the imaging region of the body

Diffusion MRI Sequence

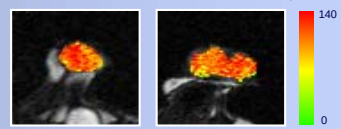
- Motion-compensated, motion-corrected, dual b-value
- TR = 2s
- field of view = 25mm^2
- image matrix = 64 x 64
- 2 averages (high b-value), single average (low b-value)

Total image time:
⇒ 6 minutes

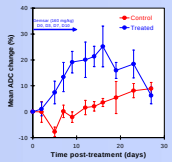
Control ADC: Day 16



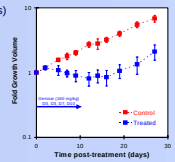
Treated ADC: Day 16



Diffusion



Volume

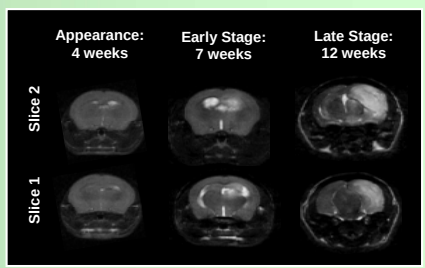


T2-weighted fast spin-echo

- 8 echo fast spin-echo
- TR=4s / TE=60 ms
- field of view = 15mm^2
- image matrix = 128 x 128
- 2 averages

Total image time:
⇒ 2 minutes

PDGF-driven Glioma in N*tv-a* Mouse



11.2 ± 0.5 minutes per mouse

Possible to image > 50 mice per day

8.2 ± 0.4 minutes per mouse