BIOGRAPHICAL SKETCH

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NAME: **Mason, Ralph P**

eRA COMMONS USER NAME (credential, e.g., agency login): RPMASON

POSITION TITLE: Professor, Radiology; Director, Small Animal Imaging Resource (SAIR), Simmons Comprehensive Cancer Center

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Churchill College, Cambridge, UK	BA	06/1983	Natural Sciences/Chemistry
Churchill College, Cambridge, UK	PhD	06/1986	*In Vivo* NMR
UT Southwestern Medical Center, Dallas, TX	Postdoctoral Fellow	06/1989	MRS/MRI

A. Personal Statement

I serve as the **Director** of the **Small Animal Imaging Shared Resource (SAISR)** at Simmons Comprehensive Cancer Center (SCCC). I am also the Director of the Cancer Imaging Program (CIP) at UT Southwestern Medical Center (UTSW) and a Professor of Radiology. I have over 25 years' experience in cancer imaging, therapy, and tumor pathophysiology. My primary research interest is prognostic radiology— developing and implementing methods for predicting optimal cancer therapy and assessing early response to treatment (precision medicine). Hypoxia is noted to be a crucial hurdle to effective radiation therapy and I continue to focus on developing, implementing and evaluating methods to effectively identify hypoxia in tumors with a view to effective translation to clinical studies in man. I have collaborated extensively with colleagues in Radiation Oncology and Urology My extensive experience with diverse imaging modalities is highlighted by the representative publications below, but here, I believe that oxygen sensitive MRI will be the most effective modality to achieve predictive imaging regarding hypoxia and its value will be demonstrated using cone beam guided irradiation of rat tumors. We have just achieved preliminary data revealing the utility of oxygen enhanced MRI to stratify tumors in terms of radiation response and see an immediate opportunity to verify these observations in other tumor types with respect to clinical magnet field and hypofractionated radiation. I am excited by the proposal to apply our pre-clinical observations to man and look forward to participating in this project. I have over 160 peer-reviewed publications with a Google h-index of 56.

1. Yu JX, Kodibagkar VD, Cui W, **Mason RP**. ^{19}F: a versatile reporter for non-invasive physiology and pharmacology using magnetic resonance. Curr Med Chem. 2005;12(7):819-48. PubMed PMID: 15853714. (cited >170 times)
2. Tatum JL, Kelloff GJ, Gillies RJ, Arbeit JM, Brown JM, Chao KS, Chapman JD, Eckelman WC, Fyles AW, Giaccia AJ, Hill RP, Koch CJ, Krishna MC, Krohn KA, Lewis JS, **Mason RP**, Melillo G, Padhani AR, Powis G, Rajendran JG, Reba R, Robinson SP, Semenza GL, Swartz HM, Vaupel P, Yang D, Croft B, Hoffman J, Liu G, Stone H, Sullivan D. Hypoxia: importance in tumor biology, noninvasive measurement by imaging, and value of its measurement in the management of cancer therapy. Int J Radiat Biol. 2006 Oct;82(10):699-757. PubMed PMID: 17118889. (cited >600 times)
3. **Mason RP**, Zhao D, **Liu L**, Trawick ML, Pinney KG. A perspective on vascular disrupting agents that interact with tubulin: preclinical tumor imaging and biological assessment. Integr Biol (Camb). 2011 Apr;3(4):375-87. PubMed PMID: 21321746; PubMed Central PMCID: PMC3071431. (cited >100 times)
4. Hormuth DA 2nd, Sorace AG, Virostko J, Abramson RG, Bhujwalla ZM, Enriquez-Navas P, Gillies R, Hazle JD, **Mason RP**, Quarles CC, Weis JA, Whisenant JG, Xu J, Yankeelov TE. Translating preclinical

MRI methods to clinical oncology. *J Magn Reson Imaging.* 2019, Nov;50(5):1377-1392. PMC6766430.

B. Positions and Honors

Positions and Employment

1997-	Member Joint Biomedical Engineering Program, UT Southwestern Medical Center and UT Arlington, Dallas, TX
1997-2002	Associate Professor, Radiology, UTSW, Dallas, TX
2003-	Professor, Radiology, UT Southwestern Medical Center, Dallas, TX
2012-	Section Chief, Preclinical Imaging, Radiology, UT Southwestern Medical Center, Dallas, TX
2010-	Director, Small Animal Imaging Shared Resource, Simmons Comprehensive Cancer Center, UT Southwestern Medical Center, Dallas, TX

Other Experience and Professional Memberships

Ongoing	Member, International Society of Magnetic Resonance in Medicine *Ad hoc* Reviewer: DOD Prostate and Breast Cancer Initiatives; NIH (P01, T32, Microscopic Imaging; SBIR, ICMIC); Mary Kay Ash Charitable Foundation; Cancer Res UK, Dutch Cancer Soc; Diabetes UK; Cancerinnovation of European Research Council; MRC UK; Wellcome Foundation; Stichting tegen Kanker (Belgium); United States - Israel Binational Science Foundation; French National Research Agency (ANR)
2003-2016	Member, Molecular Biophysics Graduate Program, UT Southwestern Medical Center, Dallas, T
2003-	Member, Simmons Comprehensive Cancer Center, UT Southwestern Medical Center, Dallas,
2009-	Member, Cancer Biology Graduate Program, UT Southwestern Medical Center, Dallas, TX
2010-2014	Reviewer, Charter Member, NIH Radiation Therapeutics and Biology Study Section
2016-2019	External Advisory Board, MD Anderson Imaging Resource

Honors

2010	Fellow, Royal Society of Chemistry, FRSC, CSci, CChem
2015	Chair, MR of Cancer Study Group, International Society of Magnetic Resonance in Medicine
2015	Famous Scientists Lecturer and Visiting Professor, Hubei University of Medicine, Shiyan, Hubei Province, China
2016	Outstanding Teacher Award: International Society for Magnetic Resonance in Medicine, ISMRM (Singapore)
2017	Outstanding Teacher Award: International Society for Magnetic Resonance in Medicine, ISMRM (Hawaii)
2021	Secretary-elect MR and Radiation Therapy study group, International Society of Magnetic Resonance in Medicine

C. Contributions to Science

1. **Developing noninvasive prognostic biomarkers of tumor hypoxia**. This primary research interest was inspired by three motivating factors: 1) reports of tumor oxygenation in human clinical subjects based on electrodes (Eppendorf Histograph) indicating that hypoxia was associated with poor prognosis in multiple disease sites; 2) reports that ^{19}F MRI of perfluorocarbon emulsion allowed interrogation of tissue pO_2 non-invasively; and 3) the increasing availability of diverse therapies that could be tailored to hypoxia, potentially allowing personalized “precision” therapy. My early work exploited perfluorocarbon emulsions such as Oxygent (perfluorooctylbromide), which was entering clinical trials as a blood substitute. We were able to show uptake in tumors and measure tumor pO_2 revealing progressive hypoxiation with tumor growth. However, signal to noise was poor due to predominant uptake by the RES and the multiple resonance characteristic of such reporter molecules. I identified hexafluorobenzene as a novel pO_2 reporter *in vivo (a)*. The single resonance provides optimal signal to noise. The spin lattice relaxation rate is exceptionally responsive to pO_2, while being minimally responsive to variation in temperature. HFB is essentially inert and clears from the body within hours. We demonstrated the ability to measure pO_2 and perhaps more importantly pO_2 dynamics in response to acute interventions based on *FREDOM* (Fluorocarbon Relaxometry using Echo planar imaging for Dynamic Oxygen Mapping) (b). We went on to show that measurements were comparable to electrode measurements, but with the great advantage that sequential repeated measurements were noninvasive and could provide maps of 50–150 individual locations in a tumor

simultaneously with a precision of 1-3 Torr (in relatively hypoxic regions) in 6.5 mins. We applied the method to explore diverse sublines of the Dunning R3327 tumor system (c). We demonstrated that pO_2 measurements and modifications of hypoxia are related to radiation response (d).

a. **Mason RP**, Rodbumrung W, Antich PP. Hexafluorobenzene: a sensitive ^{19}F NMR indicator of tumor oxygenation. NMR Biomed. 1996 May;9(3):125-34. PubMed PMID: 8892399. (cited ≥90 times)
b. Hunjan S, Zhao D, Constantinescu A, Hahn EW, Antich PP, **Mason RP**. Tumor oximetry: demonstration of an enhanced dynamic mapping procedure using fluorine-19 echo planar magnetic resonance imaging in the Dunning prostate R3327-AT1 rat tumor. Int J Radiat Oncol Biol Phys. 2001 Mar 15;49(4):1097-108. PubMed PMID: 11240252. (cited ≥130 times)
c. Zhao D, Constantinescu A, Hahn EW, **Mason RP.** Differential oxygen dynamics in two diverse Dunning prostate R3327 rat tumor sublines (MAT-Lu and HI) with respect to growth and respiratory challenge, *Int. J. Radiat. Oncol. Biol. Phys*., 53 (3), 744-756 (2002). PubMed PMID: 12062621. (cited ≥35 times)
d. Zhao D, Constantinescu A, Chang CH, Hahn EW, **Mason RP**. Correlation of tumor oxygen dynamics with radiation response of the Dunning prostate R3327-HI tumor. Radiat Res. 2003 May;159(5):621-31. PubMed PMID: 12710873. (cited ≥49 times).

2. **Studies of ^{19}F MRI of hexafluorobenzene as an effective quantitation standard for evaluating tumor oxygenation.** This method requires direct intratumoral delivery and is invasive, albeit minimally. Achieving IND approval for use in humans would be difficult and ^{19}F MRI remains esoteric on clinical scanners. Thus, we sought more practical solutions. An NCI-sponsored workshop on tumor oxygenation prompted me to investigate whether BOLD (Blood Oxygen Level Dependent) contrast might provide noninvasive insights into tumor oxygenation, as exploited for fMRI of the brain. In studies of syngeneic rat breast tumors, we showed that those tumors showing a large (> 3%) BOLD response to oxygen breathing challenge had essentially no residual hypoxia, whereas tumors with a small response had considerable residual hypoxia (a). We went on to demonstrate that such BOLD measurements are feasible in tumors at various disease sites in human patients (*e.g.*, cervix, breast, brain, prostate, and lung) (b). However, vascular delivery of oxygen does not necessarily define increased pO_2, since oxygen could simply be consumed. The work of Matsumoto *et al.* at NIH prompted us to explore interleaved BOLD and TOLD (T_1-sensitive Tissue Oxygen Level Dependent contrast) with respect to hyperoxic gas challenge (c). We found robust correlations with ^{19}F based oximetry as well as relationship to tumor response to radiation. Recently, we have explored technical subtleties of oxygen- sensitive MRI, such as a counter-intuitive TOLD response to hypoxic gas breathing change, emphasizing the importance of combined BOLD and TOLD measurements (d).
   a. Zhao D, Jiang L, Hahn EW, **Mason RP**. Comparison of ^{1}H blood oxygen level-dependent (BOLD) and ^{19}F MRI to investigate tumor oxygenation. *Magn Reson Med*. 2009 Aug;62(2):357-64. PubMed Central PMCID: PMC4426862. (cited >60 times)
   b. Zhou H, Hallac RR, Yuan Q, Ding Y, Zhang Z, Xie XJ, Francis F, Roehrborn CG, Sims RD, Costa DN, Raj GV and **Mason RP.** Incorporating Oxygen-Enhanced MRI into Multi-Parametric Assessment of Human Prostate Cancer. *Diagnostics* **2017**, *7*(3), 48; PubMed Central PMCID: PMC5617948.
   c. Hallac RR, Zhou H, Pidikiti R, Song K, Stojadinovic S, Zhao D, Solberg T, Peschke P, **Mason RP**. Correlations of noninvasive BOLD and TOLD MRI with pO_2 and relevance to tumor radiation response. *Magn Reson Med.* 2014 May;71(5):1863-73. PubMed Central PMCID: PMC3883977. (cited ≥65 times)
   d. Yang DM, Arai TJ, Campbell JW III, Gerberich JL, Zhou H, and **Mason RP**, Oxygen-Sensitive MRI Assessment of Tumor Response to Hypoxic Gas Breathing Challenge, *NMRBiomed*, 32(7):e4101 2019 DOI:10.1002/nbm.4101. PubMed PMID: 31062902.

3. **Applications of imaging to radiation response**. Initially we examined a single high dose of x-rays on subcutaneous prostate tumors. Recently, we have reported investigations using fractionated irradiation (a). We have also collaborated with investigators exploring alternate high LET irradiation; notably, carbon beam with the group in Heidelberg with evidence suggesting that heavy ions will be more relevant to hypoxic tumors (b). Oxygen sensitivity may be modeled (c). We also note that oxygen enhanced MRI is not always optimal for predicting response to radiation; notably, for tumors that did not respond to an oxygen breathing challenge, more traditional DCE MRI was associated

with tumor growth delay (d).

a. White DA, Zhang Z, Li L, Gerberich J, **Stojadinovic S**, Peschke P, **Mason RP.** Developing Oxygen-Enhanced Magnetic Resonance Imaging as a Prognostic Biomarker of Radiation Response, *Cancer Letters,* 380, 69–77 (2016). PubMed Central PMCID: PMC4967391.
b. Glowa C, Karger CP, Brons S, Zhao D, **Mason RP.** Huber PE, Debus J, Peschke P, Carbon ion radiotherapy decreases the impact of tumor heterogeneity on radiation response in experimental prostate tumors, *Cancer Letters* 378, (2) 97–103 (2016) PubMed PMID: 27224892.
c. Belfatto A., White D.A., **Mason RP**, Zhang Z., Stojadinovic S**.**, Baroni G., and Cerveri P., "Tumor radio-sensitivity assessment by means of volume data and magnetic resonance indices measured on prostate tumor bearing rats," *Med. Phys.* 43, 1275 (2016); doi: 10.1118/1.4941746 PubMed Central PMCID: PMC5148178
d. Hallac R, Zhou H, Pidikiti R, Song K, Solberg T, Kodibagkar V, Peschke P and **Mason RP.** A role for dynamic contrast enhanced magnetic resonance imaging in predicting tumor radiation response, *Br. J. Cancer*, 114(11):1206-11. | doi: 10.1038/bjc.2016.1102016 (2016). PubMed Central PMCID: PMC4891499.

4. **Extending applications of MRI to tumor irradiation**. We have extended investigations to more complex tumor models including orthotopic sites such as prostate (a) and lung (b, c, d).
   a. Chiu T.D., Arai T.J., Campbell III J., Jiang S.B., **Mason RP**, and Stojadinovic S., "MR-CBCT Image-Guided System for Radiotherapy of Orthotopic Rat Prostate Tumors", *PLoSONE*, 1-19, May 30, 2018 PubMed Central PMCID: PMC5976174
   b. Zhou H., Zhang Z., Denney R., Williams J.S., Gerberich J., Stojadinovic S., Saha D., Shelton J.M., and **Mason RP**, "Tumor physiological changes during hypofractionated stereotactic body radiation therapy assessed using multi-parametric magnetic resonance imaging" *Oncotarget*, 8: 37464-37477, (2017) PubMed PMCID: PMC5514922
   c. Zhang Z, Wodzak M, Belzile O, Zhou H, Sishc B, Yan H, Stojadinovic S, **Mason RP**, Brekken RA, Chopra R, Story MD, Timmerman R and Saha D. Effective Rat Lung Tumor Model for Stereotactic Body Radiation Therapy, *Radiat. Res.* 2016 Jun;185(6):616-22. doi: 10.1667/RR14382.1. Epub 2016 May 25. PubMed Central PMCID: PMC4966888.
   d. Zhou H., Belzile O., Zhang Z., Wagner J., Ahn C., Richardson J.A., Saha D**.**, Brekken R.A. and **Mason RP**, "The effect of flow on BOLD (R_2*) MRI of orthotopic lung tumor" *Magn. Reson. Med.*, Magn Reson Med. 81:3787–3797 2019 PubMed PMCID: PMC6527131

5. **Novel imaging applications with diverse modalities** (a) including optical (b, c) and most recently photoacoustic (d).
   a. N. J. Serkova, K. Glunde, C. R. Haney, M. Farhoud, A.DeLille, E. F. Redente, D. Simberg, D. C. Westerly, L. Griffin, **Mason RP**, Preclinical Applications of Multi-Platform Imaging in Animal Models of Cancer, Cancer Res., online 1Dec 2020 doi: 10.1158/0008-5472.CAN-20-0373 PMID: 33262127
   b. Paroo Z, Bollinger RA, Braasch DA, Richer E, Corey DR, Antich PP and **Mason RP**, Validating bioluminescence imaging as a high-throughput, quantitative modality for assessing tumor burden. *Molecular Imaging*, 3, 117-124 (2004), PubMed PMID: 15296676. (cited ≥110 times)
   c. Liu L and **Mason RP.** Imaging β-galactosidase activity in human tumor xenografts and transgenic mice using a chemiluminescent substrate, *PloS ONE* 5(8): e12024, Online August 6, 2010. PubMed Central PMCID: PMC2917367
   d. D. O'Kelly,Y. Guo, and **R. P. Mason**, "Evaluating Online Filtering Algorithms to Enhance Dynamic Multispectral Optoacoustic Tomography" *Photoacoustics*, 2020 2020 May 16;19:100184. PubMed PMCID: PMC7264082

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/pubmed/?term=Ralph%20Mason

D. Research Support
Ongoing Research Support

1R01CA244579-01A1 Mason/Pinney (PI) 07/01/20 – 06/30/25
NIH/NCI
Vascular image-guided optimization of response (VIGOR) to therapy in kidney cancer
The goal is to develop the application of a novel vascular disrupting agent (VDA) in combination with leading therapies to enhance treatment of renal cell carcinoma (RCC) and improve tumor control.
Role: Multi- PD/PI

T32EB028093 Mattrey (PI) 05/01/19-04/30/24
NIH/NIBIB Training Grant
The goal of this study is training clinician scientists as outstanding clinician and imaging scientists.
Role: Mentor

RP200021 Zhang/Liu (PI) 03/01/20-02/28/23
Cancer Prevention and Research Institute of Texas
Optimizing Therapeutic Strategies Against Lung Cancer Using Multi-Modality Imaging
The goal is to determine the degree to which CycT (cyclopamine tartrate) and HSP2 (heme-sequestering peptide 2) alleviate tumor hypoxia and normalize tumor vasculature
Role: Co-Investigator

1653474 Lippert (PI) 07/01/17-06/30/22
Southern Methodist University/National Science Foundation
CAREER: Triggered Energy Transfer Chemiluminescence for *In Vivo* Imaging
The goal of this study is to develop novel chemiluminescent reporter molecules to study physiology.
Role: Role: PI Subcontract

T32 HL134613 Nguyen (PI) 07/01/17-06/30/22
NIH/NHLBI Training Grant
The goal of this study is to train bioengineering trainees in nanotechnology and cardiovascular and lung diseases.
Role: Mentor

P30CA142543 Arteaga (PI) 08/01/15-07/31/21
NIH/NCI
UT Southwestern Cancer Center Support Grant
The goal of this project is to support the infrastructure for the promotion of interdisciplinary, translational cancer research through the efforts of senior leadership, five scientific research programs, six shared resources, protocol specific research, protocol review and monitoring, planning and evaluation activities, developmental funds, community outreach and engagement, education and training, and administration.
Role: Director, Small Animal Imaging Resource

R21 CA243255 Cheng (PI) 07/01/19-06/30/21
NIH/NCI
Massachusetts General Hospital (PA-16-040)
Probing Prostate Cancer Bioactivity with Polyamine Dynamics
The goal is to develop hyperpolarized polyamine substrates as metabolic indicators of prostate cancer.
Role: Co-Investigator, PI sub-contract

Selected Completed Research Support

R44 CA144817 Unger (PI) 09/12/17-08/31/20
NIH/NCI
Randomized Prospective Phase II Clinical Trial of NVX-108 in Association with Chemoradiation NUVOX PHARMA LLC
The goal was to develop a safe, nanotechnology product that, following IV administration, raises oxygen levels in tumor tissue to improve response to radiation and survival outcomes in these patients.
Role: Co-Investigator