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TITLE: **Characterizing the Aggressiveness of Prostate Cancer with Multimodality Imaging**

PRINCIPAL INVESTIGATOR: Prof. Timothy J. Scholl

CONTRACTING ORGANIZATION: The University of Western Ontario

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<b>13. SUPPLEMENTARY NOTES</b>					
<b>14. ABSTRACT</b> The goal of this research project is to demonstrate the ability of multimodality imaging to improve detection of prostate tumors and accurately determine their aggressiveness by comparing non-invasive molecular imaging to pathological examination. This project will study a total of 45 men with biopsy-proven prostate cancer. Prior to prostatectomy, they will undergo molecular imaging. After prostatectomy, sections of their prostates will be examined under a microscope by a pathologist. This examination is the gold-standard for characterizing tumors and will be used to establish how accurately the pre-surgical multimodality imaging assay was able to find tumors and predict their aggressiveness.					
<b>15. SUBJECT TERMS</b> prostate cancer, multi-modality imaging, MRI, PET, tissue sodium concentration, prostate specific membrane antigen, prostatectomy biopsy, tumour aggressiveness, Gleason grade					
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## 1. INTRODUCTION:

The purpose of this research is to demonstrate the ability of multimodality imaging to improve detection of prostate tumors and accurately determine their aggressiveness by comparing non-invasive molecular imaging to pathological examination. This project will study a total of 45 men with biopsy-proven prostate cancer. Prior to prostatectomy, they will undergo molecular imaging. After surgery, sections of their prostates will be examined under a microscope by a pathologist.

## 2. KEYWORDS:

prostate cancer, magnetic resonance imaging, positron emission tomography tissue sodium concentration prostate specific membrane antigen, prostatectomy, histopathology, tumour aggressiveness, Gleason grade

## 3. ACCOMPLISHMENTS:

**What were the major goals of the project?**

- 1) Evaluation of dual frequency proton/sodium MRI RF hardware for prostate imaging (completed, 12/2020)
- 2) Evaluation of non-Cartesian pulse sequence for sodium MRI (completed, 12/2020)
- 3) Redesigned external RF hardware for sodium-MRI (completed 06/2022)
- 4) Manuscript preparation dissemination results of 1), 2) and 3) (in preparation, 09/2023)
- 5) Recruitment of patients for imaging study (Recruitment is underway but delayed due to restrictions on research at Canadian hospitals during COVID-19. To date, 14 of 45 men have been recruited.)
- 6) Multivariate analysis (awaiting completion of recruitment)
- 7) Dissemination of study results (to be completed at end of study)

**What was accomplished under these goals?**

We have recruited 14 men into our research study, and they have been imaged with multi-parametric MRI, sodium-MRI and PET using the latest prostate cancer tracer, PSMA-1007, which is now being manufactured at the Nordal Cyclotron and PET Radiochemistry Facility at the Lawson Health Research Institute. Histological examination of the prostate tissue has been completed for these subjects. We constructed an external transmit/receive butterfly RF coil, which eliminates the insertion of an endorectal receive RF coil for sodium-MRI. The new RF hardware produces uniform signal assessment throughout the entire prostate, and it is much better tolerated than the endorectal coil. Development of the non-invasive RF coil for sodium-MRI has decreased the concerns of discomfort for men considering participating in this study and improved subject accrual.

**What opportunities for training and professional development has the project provided?**

This project is providing training for:

- 1) Ms. Josephine Tan, a Doctoral student currently supervised by Prof. J. Thiessen and T. Scholl. This student presented this research at three international conferences (see below).
- 2) Dr. Alireza Akbari, a Research Scientist currently supervised by T. Scholl. This individual has received mentorship and attended conference workshops focused on sodium magnetic resonance imaging.

**How were the results disseminated to communities of interest?**

Nothing to Report.

**What do you plan to do during the next reporting period to accomplish the goals?**

We are doubling our efforts to increase patient uptake for our study this includes recruitment from the surgical practice of four urological surgeons including a recently recruited surgeon, Dr. Brant Inman. We have developed and implemented a non-invasive RF coil for measurement of tissue sodium concentration throughout the entire prostate. We expect that replacing the endorectal RF coil with this new external RF coil will improve uptake of patients who were concerned with possible discomfort of the internal coil during an hour-long imaging session.

**4. IMPACT:**

*What was the impact on the development of the principal discipline(s) of the project?*

We have demonstrated the ability to non-invasively measure tissue sodium concentration (TSC) throughout the entire prostate. We have acquired TSC data and multiparametric proton MR imaging data simultaneously with positron emission tomography using PSMA-1007 (a tracer that binds to prostate specific membrane antigen, which is over-expressed in prostate cancer. Biomarkers from these data have been extracted for comparison with cancer aggressiveness determined from histological examination after prostatectomy.

**What was the impact on other disciplines?**

Nothing to Report.

**What was the impact on technology transfer?**

Nothing to Report.

**What was the impact on society beyond science and technology?**

Nothing to Report.

**5. CHANGES/PROBLEMS:**

In 2020, we have changed the original radio-labeled PET tracer from [18F]DCFPyL to PSMA-1007, which is now being manufactured locally at our own cyclotron (Nordal Cyclotron and PET Radiochemistry Facility, Lawson Health Research Institute) under license from the Centre for Probe Development and Commercialization (CPDC) in Hamilton, ON. Local production of this agent improves the access to this agent so that it is available to us on a weekly schedule to assist with patient recruitment schedule conflicts. As mentioned above, we are now using an external RF coil for sodium-MRI to reduce patient anxiety with possible discomfort of the placement of an endorectal RF coil.

**Actual or anticipated problems or delays and actions or plans to resolve them**

Compared with the experience in the United States, the effects of COVID-19 from 2020 – 2022 was much more significant on the socialized healthcare system in Canada. The impact on this research project was severe as hospital surgeries including prostatectomies were shelved, and men with prostate cancer were placed on hormone therapy as an interim step toward eventual intervention. Recruitment to our study during this period was severely hampered by this lack of prostate surgeries and the hesitancy of patients to participate in our study even as the COVID crisis abated. While hormone therapy is obviously helpful for the patient, it makes accurate Gleason grading of the disease after prostatectomy impossible. As a result, these men were not eligible for our study as we require whole-mount histopathology as our gold-standard for comparison with MRI and PET imaging data. The province has subsequently provided additional funding to reduce surgical wait times and reduce the backlog of men awaiting treatment. This has aided accrual to this imaging study. Additionally, we have developed an external RF coil system during the COVID shutdown to replace the endorectal RF coil mitigating any discomfort, which was a concern for men who were considering participation in our study. A further benefit of our new RF coil is that it now provides uniform detection of sodium concentration throughout the entire prostate, while previously, our imaging sensitivity was limited to the peripheral zone of the prostate where 80% of all lesions are typically found.

**Changes that had a significant impact on expenditures**

None.

**Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**

**Significant changes in use or care of human subjects**

None.

**Significant changes in use or care of vertebrate animals**

None. No animals were involved in this study.

**Significant changes in use of biohazards and/or select agents**

None.

## 6. PRODUCTS:

- **Publications, conference papers, and presentations**

### **Journal publications.**

#### **Peer-Reviewed Journal Publication (In preparation)**

Tan, JL, Thiessen JD, Scholl TJ, and Akbari A; **Development of an external butterfly coil for sodium MRI of human prostate cancer**; NMR in Biomedicine (other); acknowledgement of federal support (yes).

#### **International Conference Presentations**

Tan, JL. **Comparison of external butterfly and endorectal coils for sodium MRI of human prostate cancer**. *Accepted for poster presentation*. World Molecular Imaging Congress (WMIC), Miami, FL. Sep 2022.

Tan, JL. **Multiparametric MRI, sodium MRI and PSMA PET of prostate cancer with histological validation of Gleason grade**. *Poster presentation*. International Society for Magnetic Resonance in Medicine Conference, London, United Kingdom. May 2022.

Tan, JL. **Characterization of Human Prostate Cancer using Non-Invasive Molecular Imaging**. *Poster Presentation*, World Molecular Imaging Congress. Virtual. Oct 2021.

**Books or other non-periodical, one-time publications.**

None.

**Other publications, conference papers and presentations.**

Tan, J.L. **Multiparametric MRI, sodium MRI and PSMA PET of prostate cancer with histological validation of Gleason grade.** *Oral presentation.* London Imaging Discovery Day, London, ON. Jun 2022.

Tan, J.L. **Characterization of Human Prostate Cancer using Non-Invasive Molecular Imaging.** *Poster Presentation,* Department of Oncology Research & Education Day, Virtual Jun 2021.

- **Website(s) or other Internet site(s)**

None.

- **Technologies or techniques**

We have developed two different RF systems for sodium-MRI of the prostate.

- 1) transmit-only volume birdcage RF coil integrated with a receive-only endorectal RF coil
- 2) transmit/receive external butterfly surface RF coil.

We have found that the non-invasive external butterfly RF coil is better tolerated by the patients.

- **Inventions, patent applications, and/or licenses**

None.

- **Other Products**

None.

## 7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

<b>Name:</b>	Timothy Scholl, PhD (no change)
<b>Name:</b>	Jonathan Thiessen, PhD (no change)
<b>Name:</b>	Glenn Bauman, MD (no change)
<b>Name:</b>	Aaron Ward, PhD (no change)
<b>Name:</b>	Stephen Pautler, MD (no change)
<b>Name:</b>	Alireza Akbari, PhD (no change)
<b>Name:</b>	Josephine Tan, MSc (no change)
<b>Name:</b>	Catherine Hildebrand, PhD (no change)
<b>Name:</b>	Mena Gaed, MD
<b>Project Role:</b>	Pathology (2019-present) and <i>Patient Recruitment (2021-present)</i>
<b>Researcher Identifier:</b>	None
<b>Nearest person month worked:</b>	12
<b>Contribution to Project:</b>	Patient recruitment, pathology, and lesion grading

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to Report.

**What other organizations were involved as partners?**

Organization Name: Ontario Institute for Cancer Research

Location of Organization: Toronto, Ontario, Canada, M5G 0A3

Partner's Contribution to the Project: Prof. Scholl is an Investigator with OICR and receives salary support from this organization.

**8. SPECIAL REPORTING REQUIREMENTS**

**COLLABORATIVE AWARDS:** *N/A*

**9. QUAD CHARTS:** *N/A*

**10. APPENDICES:** *N/A*