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General Information

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Are external grants or funds being used to support this research?: No external grants or funds are being used to support this research.

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Certification

Certification: Yes
Data Use Agreement Training: As the Principal Investigator of this study, I certify that I have completed the YODA Project Data Use Agreement Training

Associated Trial(s): [NCT00638690 - A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study of Abiraterone Acetate \(CB7630\) Plus Prednisone in Patients With Metastatic Castration-Resistant Prostate Cancer Who Have Failed Docetaxel-Based Chemotherapy](#)

What type of data are you looking for?: Full CSR

Research Proposal

Project Title

Is primary tumor in prostate cancer a reliable target lesion (measurable disease) at contrast-enhanced (CE) CT.

Narrative Summary:

Radiographic assessment of treatment response or disease progression in metastatic prostate cancer (PCa) is limited due to the lack of measurable lesions. In PCa, measurable disease is essentially limited to lymph node metastases which occur only in 20-25% of patients and can be a poor reflector of disease status. Bone metastases are non-measurable and other metastases in PCa are rare. In most other cancers, the primary tumor is assessed during imaging follow up to determine treatment effect. Two recent studies have concluded that the dominant tumor in PCa can be accurately detected at routine CECT. This study assesses whether primary tumor in metastatic PCa can be used as a target lesion.

Scientific Abstract:

Background.

Radiographic assessment of metastatic PCa is limited due to the lack of measurable lesions. Measurable disease is almost exclusively lymphadenopathy, which occurs in 20-25% of patients and can be a poor reflector of disease. Skeletal metastases are non-measurable and visceral metastases are rare. Recent studies have concluded that primary tumor in PCa can be detected accurately with routine CECT.

Objective.

To determine if primary tumor can be used as a target lesion at routine CECT to improve radiographic assessment of metastatic PCa.

Study design.

Retrospective cohort study, where two blinded abdominal radiologists will independently review baseline and follow-up CECT examinations (assessing conventional targets and primary tumor) in metastatic PCa and record all measurable lesions. Re-staging accuracy (with and without measurements of primary tumor) will be compared to other markers of treatment response.

Participants.

Patients with metastatic castrate resistant prostate cancer and without prostatectomy.

Main Outcome Measure(s):

1. Assessment of treatment response using CECT with and without measurement of primary tumor compared to other defined outcome measures.
2. Inter-observer agreement for measurable lesions including primary tumor.

Statistical Analysis.

1. Accuracy of re-staging: Measurements with/without primary tumor will be correlated to outcomes of treatment response using Spearman/Pearson Correlation and modeling.
2. Inter-observer agreement: Cohen's Kappa and Bland-Altman Analysis.

Brief Project Background and Statement of Project Significance:

Re-staging of patients with metastatic PCa is challenging. There is a lack of measurable lesions in PCa compared to other cancers. For most cancers, radiographic assessment is quantified according to the Response Evaluation Criteria In Solid Tumors (RECIST) (version 1.1). The limitations of RECIST 1.1 in PCa have been well documented [1; 2], because assessment is typically limited to bone and lymph nodes [3-8]; with visceral disease occurring less commonly [9]. Osseous metastases are non-measurable in RECIST 1.1 [10] and nodal metastases occur in 20-25% of patients [2]. Lymphadenopathy can also be a poor reflector of disease status [2;5; 6].

The Prostate Cancer Clinical Trials Working Group (PCWG) 2 updated the eligibility and outcome measures to evaluate systemic treatment in metastatic PCa [11]. PCWG2 recommends evaluation of disease response by RECIST 1.1 criteria with the caveat that only lymph nodes that measure up to 2.0 cm in long axis be considered measurable lesions [12]; this further limits the number of potentially measurable lesions. PCWG2 also recommends baseline imaging of the prostate gland with CT-MRI at the time of enrollment to determine if disease is present, but, does not consider the primary tumor at follow up imaging [12].

Two recent studies by Glazer et al. and Schieda et al. have concluded that Gleason score $\geq 4+3=7$ primary tumor in PCa can be detected by high degrees of accuracy and with good inter-observer agreement using routine contrast enhanced CT [12;13]. In our practice we have observed a decrease in size or disappearance of primary tumor in metastatic PCa with favorable treatment response and conversely increase in size or re-appearance of primary tumor with disease progression. This study will determine if primary tumor can be used as a measurable target lesion, potentially improving the radiographic assessment of treatment response in metastatic PCa. The outcome of this study could have direct implications in routine patient care and in clinical trials where assessment of treatment effect in metastatic PCa is limited.

Specific Aims of the Project:

Study Objective: To determine if primary tumor in metastatic prostate cancer can be used as a measurable lesion during the re-staging of patients undergoing contrast enhanced CT to improve re-staging accuracy.

Specific Aims:

1. Compare staging accuracy of CT using PCWG2 criteria to other disease outcomes such as PSA, mortality etc...
2. Compare staging accuracy of CT using PCWG2 criteria and primary tumor assessment (as defined by RECIST v1.1) to other disease outcomes.
3. Compare inter-observer agreement for assessment of primary tumor at CT during re-staging.

What is the purpose of the analysis being proposed? Please select all that apply. New research question to examine treatment effectiveness on secondary endpoints and/or within subgroup populations

Research Methods**Data Source and Inclusion/Exclusion Criteria to be used to define the patient sample for your study:**

Data Source: Patients with metastatic castrate resistant prostate cancer enrolled in the Abiraterone randomized control trial.

Inclusion criteria:

1. Metastatic Castrate Resistant Prostate Cancer.
2. Baseline contrast enhanced CT (CECT)
3. At least one follow-up CECT
4. Other metrics of disease response or progression: Bone scan results, PSA response/progression, Survival, Disease Free Survival

Exclusion Criteria.

1. Prostatectomy
2. No follow up CECT examinations or CECT not performed at baseline.
3. No other metrics to compare disease response or progression.

Research Methods.

Two blinded abdominal radiologists will independently evaluate baseline and follow up CECT studies measuring all measurable lesions (as defined by PCWG2 criteria) and measuring primary tumor. Treatment response using only PCWG2 criteria and using PCWG2 criteria combined with primary tumor measurement will be compared to other outcomes of treatment response using Spearman/Pearson correlation and regression modelling. Inter-observer agreement will also be assessed to determine the agreement between measurement and detection of primary tumor.

Main Outcome Measure and how it will be categorized/defined for your study:

The main outcome measure in this study is whether the addition of measurements of dominant primary tumor in metastatic PCa improves radiographic assessment of treatment response or disease progression on follow up with CECT.

Radiographic assessment of disease response-progression will be compared with-without the use of primary tumor to other outcomes of treatment effect including PSA response/progression, survival, disease free survival

Main Predictor/Independent Variable and how it will be categorized/defined for your study:

Main Independent Variable to be assessed: Measurement of dominant primary tumor.

Measurement of primary tumor will be defined according to existing RECIST v1.1 guidelines for assessment of solid tumors. A hyper-enhancing focus in the prostate gland (as defined in the studies by Glazer and Schieda et al. [12;13]) will be considered only if it measures > 1.0 cm in long axis, according to RECIST v1.1 guidelines.

Other Variables of Interest that will be used in your analysis and how they will be categorized/defined for your study:

Other variables of interest in this study include:

1. Other measurable lesions as defined by existing PCWG2 guidelines: Lymph nodes and visceral metastases.
2. Other outcome data used as a comparative metric to determine re-staging accuracy of CECT with-without the use of primary tumor: PSA response/progression, survival, disease free survival.

Statistical Analysis Plan:

1. Assessment of Treatment response using radiographic criteria:

Score from PCWG2 will be compared to parametric and non-parametric outcomes of disease response using Pearson/Spearman correlation.

Score from PCWG2 + Primary tumor measurement (defined by RECIST v1.1) will also be compared to other outcomes of disease response using correlation.

Uni-variate regression modeling of primary tumor measurement and Multi-variate regression modeling with-without primary tumor measurement will be compared to other treatment outcomes.

Project Timeline:

Anticipated project start date: 4 weeks after access to CT data provided.

Anticipated time to completion of CT interpretations (including baseline and follow-up CECT studies): 8-12 weeks

Anticipated time for statistical analysis: 2-4 weeks

Anticipated time for manuscript drafting and submission for publication: 6-8 weeks after study completion and statistical analysis.

Total time to completion of project and submission of manuscript: 20-28 weeks

Dissemination Plan:

Anticipated target audience:

Radiologists, Medical-Radiation and Surgical Oncologists involved in the management of PCa

Anticipated Conference for presentation of work:

Radiological Society of North America Annual Scientific Meeting

Anticipated Journal for Submission:

1. Cancer (or similar medical oncologic journal), International Journal of Radiation Oncology*Biography*Physics
2. Radiology or European Radiology

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