TITLE:
Dose Intensification with a Focal Boost to Dominant Intraprostatic Lesion using Volumetric Modulated ArcTherapy /Image Guided Radiotherapy in Patients with Localized Prostate Cancer

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ABSTRACT:
Prostate cancer is a multi-focal disease and conventional therapies address this by treating the whole gland. However, numerous evidence coming from prostate pathology studies suggest the existence of a dominant cancer focus or dominant lesion (DL) within the gland that may be the nucleus of the aggressiveness of the cancer and therefore of recurrence post treatment. Thus strategies to identify and intensify treatment to this DL are under active investigation. Advances in multiparametric magnetic resonance imaging (mpMRI) have shown promising results in identifying focal lesions and advances in high accuracy radiotherapy have enabled dose intensification.

Hypothesis
The hypothesis is that differential boosting with focal dose escalation delivered by VMAT to an imaging (mpMPR) defined DL within the prostate is associated with a higher PSA, clinical (mpMRI) and histological control without a significant increase in toxicity (both acute and late) in males with localized prostate.

Objectives
The aim of this study was to determine the efficacy and safety of the implementation of a program of " image-guided focal Intensification dose to intraprostatic dominant lesion " in men with localized prostate cancer (PCa) of intermediate and high risk (criteria NCCN) eligible to receive radiotherapy in the Department of Radiation Oncology of HUP within the established dose escalation protocol with intensity modulated image-guided radiotherapy (IMRT / IGRT).

Primary objectives:
- To increase biochemical and local control of patients localized PCa of intermediate and high- risk.
- To maintain or decrease the incidence of acute and late urinary rectal complications despite increased dose (focal) radiotherapy.

Secondary objectives:
- Biochemical disease-free survival at 3 yrs (according to RTOG-ASTRO Phoenix Consensus Conference criteria).
- Assessment of the quality of life perceived by the patient in the urinary, digestive and hormone domains.
- To determine the impact of treatment on the disease-free survival (DFS).

- To assess the adequacy of the safety margins of the treatment volume and the possibility of reducing these margins to minimize the risk of complications when incorporating specific immobilization.

SAMPLE SIZE 37 PATIENTS

STUDY VARIABLES DEFINITION

1. Patients were counted as biochemical failures according to the Phoenix definition (PSA >2 ng/mL above the currently observed PSA nadir). The Kaplan- Meier method was used to estimate the probability of biochemical control and of DFS.
2. Biochemical relapse-free survival (bRFS) was calculated from the time of first radiation treatment to failure, last follow-up or death. PSA nadir was set to be the lowest PSA value following treatment completion. Benign bounce was defined as nadir +0.2 ng/ml as long as subsequent PSAs after the bounce dropped lower than the relative nadir before the bounce.
3. Morphological and functional response was evaluated by mpMRI at 12 months after radiotherapy and compared to the baseline scans.
4. Acute toxicity was assessed in terms of the incidence and severity of genitourinary (GU) and gastrointestinal (GI) adverse events from 48 h until 3 months after the procedure.
5. Late toxicity defined as the maximal toxicity per patient more than 90 days after completion of RT Late adverse effects of radiation assessed at each follow-up visit using the radiation morbidity scoring criteria of the European Organization for Research and Treatment of Cancer Radiation Therapy Oncology Group (EORTC/RTOG) and The Common Terminology Criteria for specific Adverse Events.

The incidence of late adverse effects was calculated as the occurrence of the maximum grade toxicity per patient divided by the number of patients in each arm. The c2 or Fisher exact test was used to evaluate differences in patient and treatment characteristics for categorical variables. The t test, analysis of variance, or Mann-Whitney test was used, depending on the type and distribution of the variables, to evaluate differences in patient and treatment characteristics for continuous data. The cumulative incidence method was used to estimate time to late toxicity, and treatment groups were compared using the log-rank test. Death from any cause was considered a competing risk.