Development of a Decision Support System in Oncology for Prostate Adenocarcinoma

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***Abstract*—** The present paper introduces a Decision Support System, applied to assessment and treatment in Oncology, named Oncology Custom Assistance Tools (OnCATs). It is aimed to evaluate if OnCATs can characterize a patient into a definitive risk group, assess all the available treatment options and individually prescribe every treatment that is part of the chosen treatment course. On the first phase the knowledge base was built resorting to 23 guidelines for the treatment of prostate cancer. The interface was built using Microsoft Visual Studio 2010. Lastly, the system was tested using 10 case reports published on the Journal of Medical Case Reports and PubMed websites. The OnCATs' output was submitted to a pass/fail analysis. OnCATs can accurately assign a risk group to a prostate cancer patient. As for treatment course assessment, it was found that the estimation of the patient's life expectancy can highly impact the output generated by the system. Regarding the prescription of treatments, OnCATs performed better on the prescription of EBRT treatments, in comparison with ADT.

***Keywords*—** Androgen Deprivation Therapy (ADT), Clinical decision support system, Prostate cancer Radical prostatectomy, Radiotherapy.

I. Introduction

Healthcare professionals are constantly faced with new research and discoveries on the medical field and practice [1]. In Oncology, given the high heterogeneity among diseases, a greater need of providing individual healthcare measures exists, to achieve optimal results. Individualized medical practices are a constant process of decision-making, as the path followed by a patient has many different stages, with several possible courses of action each [2,3].

Healthcare professionals must make critical decisions based on a huge set of information and with limited time. This is a key opportunity for clinical Decision Support Systems (DSS). A DSS is a computerized system, which is designed to assist a healthcare professional in performing a task that involves making a set of different decisions. This technology has been globally used with the aim of saving time and reducing medical errors [4].

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The goal of this study is to develop a method of implementation for a knowledge based clinical DSS for assessment and treatment in Oncology. The developed clinical DDS was named Oncology Custom Assistance Tools (OnCATs). We also aim to test the system's algorithm and evaluate its performance and appliance to real clinical cases of prostate adenocarcinoma, by evaluating if the system can successfully characterize a patient into a definitive risk group, evaluate the available treatment courses, and prescribe every single treatment modality that constitutes the chosen treatment course.

Prostate cancer can be treated with several treatment options, such as External Beam Radiotherapy (EBRT), Brachytherapy (BT) or Radical Prostatectomy (RP). This variety of treatments produce different side effects, which can cause different impacts on the patient's quality of life. The development of these tools is also necessary to efficiently compare the predicted outcomes of different treatment courses, which plays a great part on the process of deciding a definitive treatment option for a patient [5]. Since having more treatment options available makes the task more demanding in terms of decision-making, since there are more variables that must be considered. Because of that, localized prostate cancer was chosen as the starting point for the development of OnCATs

II. Methods

To start building the system's knowledge base, a web search was conducted, including the keywords "prostate cancer", "treatment", "management" and "guidelines". This search led us to obtain a total of 23 published guidelines to incorporate on the OnCATs original knowledge base [6,7,16-18,23-28,8-15]. The obtained information was stored in tables using Microsoft Excel, according to the following criteria:

- Risk classification definition: tumor stage, Gleason Score (GS) and Prostate-Specific Antigen (PSA) value;
- Treatment course assessment: patient life expectancy, presence of symptoms and presence of tumor adverse features;
- RT prescription: total delivered dose and dose fractionation for RT treatments;
- ADT prescription: first line ADT approach and treatment duration.

The knowledge base was digitally integrated to create the system's interface, in the form of a computerized software, meant to be used on the Microsoft Windows operating system, using Microsoft Visual Studio 2010 [29]. Decision rules, as in *IF <condition> THEN <consequence>*, were applied because data stored in tables or flow chats is easy to integrate when using a decision tree workflow that supports routines, subroutines, and functions, which allows to easily convert medical knowledge in an executable workflow system.

A. System Workflow

A summary of the workflow of the OnCATs' algorithm can be consulted on fig. 1. The first stage of the OnCATS workflow is to verify to which risk group a specific patient belongs to, using the given tumor stage, GS and PSA level [6,7,25,8,11,12,14-16,18,23]. The second stage of the workflow is to assess all the available treatment options. By evaluating the patient's estimated life expectancy, presence of symptoms and presence of adverse tumor features, the system will recommend Observation, Active Surveillance (AS), ADT, BT, RP with or without Pelvic Lymph Node Dissection (PLD), or any combination of these treatment modalities. In third stage of the workflow, the system assists the prescription of each individual modality that is part of the chosen treatment course.

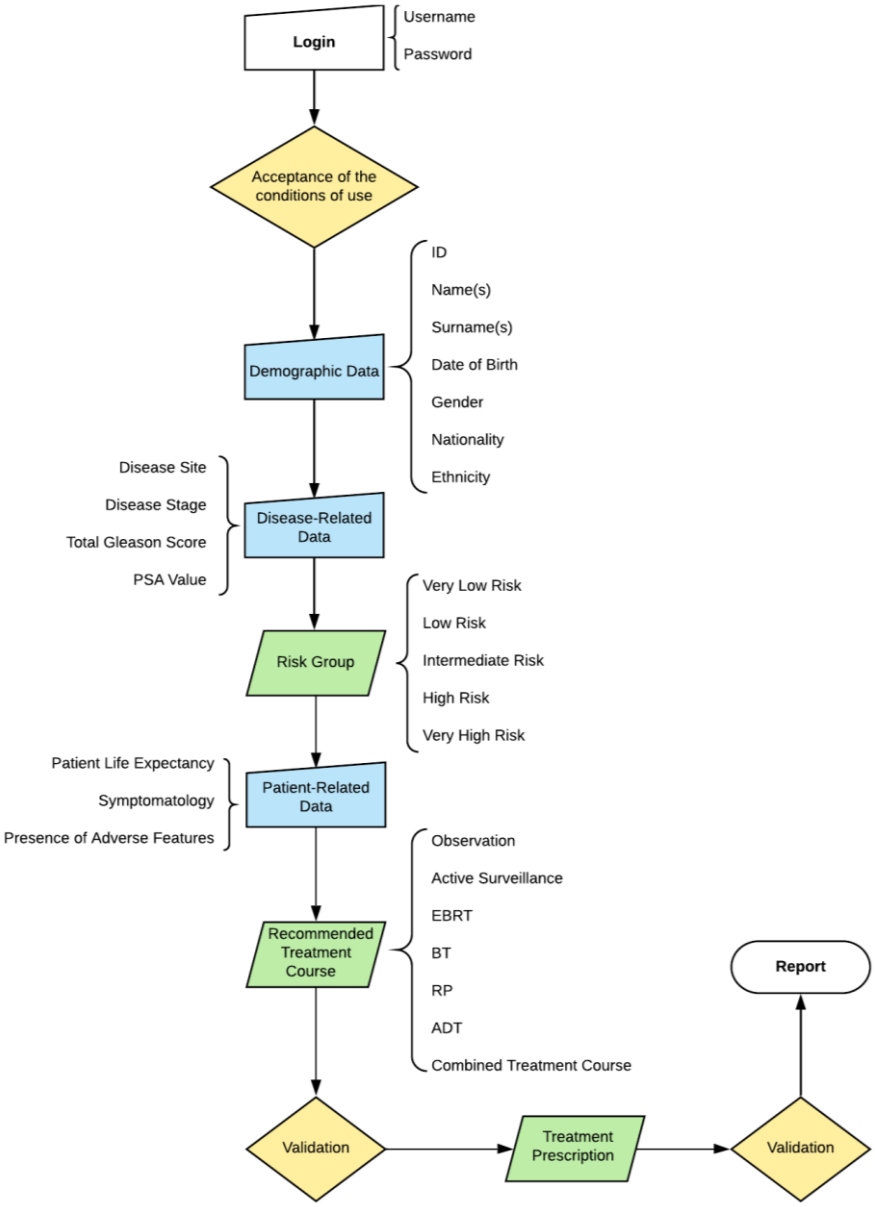

Fig. 1 Representation of the OnCATs' clinical workflow

B. System Testing

To evaluate if the OnCATs workflow could successfully simulate the clinical workflow for prostate cancer treatments, clinical cases of real patients were necessary. To obtain these cases, we recurred to the Journal of Medical Case Reports and PubMed websites, where a web search was conducted using the keywords "prostate" and "cancer" [30,31]. Using the advanced search function, we searched for articles that contained the words "prostate" and "cancer" in its title. Filters were applied to display only case reports, articles with full text available for free, published in last 5 years, and written in English. After revising all the publications, a total of 10 clinical cases were obtained.

The method of Kim et al. was applied to estimate the patients' life expectancy [32]. Regarding the quartile of health, we considered patients who had comorbidities, such as diabetes mellitus or hypertension, to not be healthy, and therefore were placed on the bottom quartile of health (bottom 25%). Patients who did not suffer from other comorbidities, were considered to be very healthy, belonging on the top quartile of health (top 25%). For the cases in which there was no mention of the presence of comorbidities, we assumed that they were overall healthy and therefore were placed on the middle quartile of health (between 25 - 75%) [32].

As for the presence of symptoms, for the clinical cases where there was no indication if the patient was symptomatic or not, we assumed the patients on lower stages were asymptomatic, while patients on higher stages were symptomatic [33]. As for defining the presence of adverse features, clinical cases where there was no mention if adverse features were present, we assumed the absence of any of these features.

A pass and fail analysis was performed to each task of the workflow. It was assumed that the system "passed" the analysis when it suggested the same approach that was applied to the patient, and it was assumed the system "failed" when different approaches were suggested. General tasks included the definition of the risk group and the evaluation of the recommended treatment approaches. RT specific tasks included the assessment of the treatment technique, dose fractionation, dose per fraction and total prescribed dose. ADT specific tasks included the assessment of the type of ADT, the first line approach and treatment duration. BT specific tasks included the assessment of the type of BT, radioactive isotope, prescribed dose and total number of fractions.

III. Results

A summary of the demographics and disease related characteristics of the clinical cases used for testing the OnCATs system can be consulted on table I. The sample of patients has a mean age of 69,7 ¬± 5,9 years (59 - 77 years) [32,34-42].

TABLE I
SUMMARY OF THE CHARACTERISTICS OF THE CLINICAL CASES USED FOR TESTING THE ONCATS' ALGORITHM

	CC01	CC02	CC03	CC04	CC05	CC06	CC07	CC08	CC09	CC10
Authors	Tisman et al.	Nishimura et al.	Hiyama et al.	Chang et al.	Coyle et al.	Tisman et al.	Brahmbhatt et al.	Shen et al.	Castro-Alonso et al.	Yamashita et al.
Year of Publication	2009	2014	2011	2016	2015	2011	2008	2019	2019	2017
Age (Years)	75	68	59	70	64	71	71	77	65	77
GS	5	7	7	9	9	7	8	9	8	6
Lead Time (Years)	10	0	0	0	0	0	0	10	0	10
Quartile of Health	Healthy	Not Healthy	Not Healthy	Not Healthy	Very Healthy	Very Healthy	Not Healthy	Healthy	Not Healthy	Healthy
Risk of Mortality by Cancer (%)	1,2	6,5	6,5	12,1	12,1	6,5	12,1	12,1	12,1	3
Life Expectancy (Years)	10,1	4,4	5,2	2,8	9,4	11,7	2,8	8,5	3,1	8,9
Life Expectancy Category (Years)	> 9	< 6	< 6	< 6	> 9	> 9	< 6	6 – 9	< 6	6 – 9

A. Risk Group Assessment

Regarding the risk group assessment, OnCATs was able to successfully characterize each patient into a risk group using the NCCN nomenclature, as demonstrated on table II [11,32,42,34-41].

According to the system's algorithm, 1 patient (10%) was characterized as having a very low risk disease, 3 patients (30%) were characterized as having intermediate risk diseases, 2 patients (20%) were characterized as having high risk diseases and 4 patients (40%) were characterized as having very high-risk diseases.

B. Treatment Course Assessment

The assessment of the available treatment courses can be consulted on table III [11,26,42,34-41].

As for the applied treatment course, 3 out of 10 patients (30 %) were submitted to radical ADT, 2 patients (20 %) were submitted to EBRT with neoadjuvant ADT, 1 patient (10 %) was submitted to radical Observation, 1 patient (10 %) was submitted with RP with PLND and adjuvant EBRT with ADT, 1 patient (10 %) was submitted to EBRT with adjuvant ADT and 1 patient (10 %) was submitted to EBRT with BT.

It was observed that the system passed in 4 out of 10 clinical cases (40 %) and failed in 6 out of 10 clinical cases

(60 %). The mean number of options that OnCATs suggested for all cases was 4,4 ¬± 1,6.

TABLE II
RESULTS OF THE RISK GROUP ASSESSMENT FOR THE CLINICAL CASES USED FOR TESTING ONCATS, USING THE NCCN NOMENCLATURE

ID	Tumor Stage	GS	PSA Value (ng/ml)	PSA Category (ng/ml)	Risk Group
CC01	T1c N0 M0	5	4	< 10	Very Low
CC02	T2b N0 M0	7	62,1	> 20	High
CC03	T2b N0 M0	7	9,5	< 10	Intermediate
CC04	T2b N0 M0	9	1,8	< 10	High
CC05	T4 N0 M0	9	< 10	< 10	Very High
CC06	T1c N0 M0	7	8	< 10	Intermediate
CC07	T4 N0 M0	8	5874	> 20	Very High
CC08	T4 N0 M0	9	52,736	> 20	Very High
CC09	T4 N0 M0	8	32	> 20	Very High
CC10	T1c N0 M0	6	10,35	10 - 20	Intermediate

TABLE III
RESULTS OF THE TREATMENT COURSE ASSESSMENT FOR THE CLINICAL CASES USED FOR TESTING THE ONCATS ALGORITHM

ID	Risk Group	Life Expectancy (Years)	Symptomatology	Adverse Features	Applied Treatment Course	Treatment Courses Suggested by OnCATs
CC01	Very Low	> 9	Asymptomatic	Present	Observation	AS EBRT RP + Observation RP + EBRT RP + EBRT + ADT
CC02	High	< 6	Symptomatic	Not Present	ADT + EBRT	EBRT + ADT EBRT + BT + ADT RP + PLND
CC03	Intermediate	< 6	Symptomatic	Present	RP + EBRT + ADT	Observation BT EBRT + ADT EBRT + BT + ADT
CC04	High	< 6	Symptomatic	Present	ADT + EBRT	EBRT + ADT EBRT + BT + ADT RP + PLND + ADT RP + PLND + EBRT + ADT RP + PLND + Observation
CC05	Very High	> 9	Symptomatic	Not Present	ADT	EBRT + ADT EBRT + BT + ADT RP + PLND
CC06	Intermediate	> 9	Asymptomatic	Present	ADT	AS BT EBRT + ADT EBRT + BT EBRT + BT + ADT RP + Observation RP + PLND + Observation RP + PLND + EBRT + ADT
CC07	Very High	< 6	Symptomatic	Present	ADT	EBRT + ADT EBRT + BT + ADT RP + PLND + ADT RP + PLND + EBRT + ADT RP + PLND + Observation
CC08	Very High	6 – 9	Symptomatic	Present	RP + PLND + EBRT + ADT	EBRT + ADT EBRT + BT + ADT RP + PLND + ADT RP + PLND + EBRT + ADT RP + PLND + Observation
CC09	Very High	< 6	Symptomatic	Not Present	EBRT + ADT	EBRT + ADT EBRT + BT + ADT RP + PLND
CC10	Intermediate	6 – 9	Asymptomatic	Not Present	EBRT + BT	Observation EBRT BT

C. Treatment prescription

For CC01, since the case report did not mention the Observation protocol that was as applied for the treatment of the patient, the comparison with the default protocol suggested by OnCATs was not possible, so further results regarding the treatment prescription for this clinical case were not possible to obtain.

1) Prescription of External Beam Radiotherapy

In general, OnCATs passed 15 out of the 20 tasks (75 %) that consisted of the workflow of CC02, CC03, CC04, CC08 and CC10. In 2 of the tasks (10%), the system failed and in 3 tasks (15 %) a comparison was not possible due to that information not being disclosed on the case report.

More specifically, regarding the treatment technique, fractionation, and dose per fraction, OnCATs was able to suggest the applied choice in all the clinical cases simulations. Regarding the dose prescription, OnCATs had a 60% passing rate, meaning that 3 out of 10 cases had a successful dose prescription and 2 cases (40 %) had a failed dose prescription.

2) Prescription of Androgen Deprivation Therapy

OnCATS managed to pass on 14 out of the 21 tasks (66,67 %) that consisted of the workflow of CC03, CC04, CC05, CC06, CC07, CC08 and CC09. In 2 of the tasks (9,52 %), the system failed and in 5 tasks (23,91 %) a comparison was not possible due to that specific information not being disclosed on the case report. More specifically, regarding the type of ADT and first line approach, OnCATs was able to successfully suggest the option applied to the clinical case in all cases (100 %). However, on the prescription of the treatment duration, in CC03 and C004, where we had indication of the total treatment duration, a comparison of results was not possible.

3) Prescription of Brachytherapy

In our sample of cases, only a single case (CC10) underwent a BT treatment. For the adjuvant BT prescription of CC10, it is possible to observe that OnCATs was able to pass on the definition of the type of BT and radioactive isotope but failed on the dose prescription and number of fractions.

4) General analysis

It is possible to observe that each clinical case had a mean passing rate of 78,7 % ¬± 15,6 %. The clinical cases where the OnCATs algorithm performed better where CC02 and CC09 (100 %), followed by CC04 (88,9 %), CC08 (85,7 %), CC05, CC06, CC07 and CC10 (75 %), CC03 (62,5 %) and CC01 (50 %).

IV. Discussion

The goal of this study was to evaluate if OnCATs could be applied to assisting decision making in all phases of prostate cancer treatment, including risk group assessment, treatment course assessment and treatment prescription, based on relevant and up-to-date clinical guidelines.

Watson for Oncology (WFO) is a DSS developed by IBM, in cooperation with the Memorial Sloan Kettering Cancer Center, whose knowledge base consists of literature, protocols and patient charts consulted on the web [44]. WFO suggest treatment options for a specific patient based on those sources, and references the evidence that support said claims [44]. WFO was found to be the developed clinical DSS most similar to OnCATs. Yu et al. conducted a retrospective study where the treatment options suggested by WFO for 201 prostate cancer patients were compared with their actual course of treatment. The authors found that the concordance rate was 73,6 %, demonstrating a high similarity between the suggestions made by the system and the treatment courses applied to the patients in the urology department of the Chonnam National University Medical School. The authors concluded that clinical DSSs can actively assist physicians on decision making, especially when expert resources are lacking, showing promise on the appliance of these tools on the Oncology workflow [44].

Regarding the few cases where OnCATs output did not match the same option that was part of the patient's course of action, it analyzed every case report in detail to investigate which reasons might have led to that occurrence.

For CC01, since Observation is reserved for older patients with one or more comorbidities that will compete with the cancer for mortality cause, the system did not suggest that option, given the estimated life expectancy for patients was 10,1 years [7,11,12,32,45]. Based on these facts, the mismatch of results could be due to the fact of the estimation of the patient's life expectancy and symptomatology not being accurate, given the missing information from the case report.

Regarding CC03, OnCATs was not able to suggest RP with adjuvant EBRT and ADT as a viable chosen treatment course. This is due to RP being more indicated to patients with an estimated life expectancy superior to 9 years, and adjuvant EBRT with ADT being reserved to patients who display adverse features [11,12,24]. Once again, the mismatch of results could be related with the estimation of the patient's life expectancy.

For CC04, regarding the ADT prescription, OnCATs was not able to suggest a treatment duration of 9 months. Based on the guidelines, for high-risk patients, the ADT treatment should be prescribed for at least 1,5 years and up to 3 years [7,11,18]. On the case report, it is stated that the patient was submitted to ADT with leuprolide for 9 months, another ADT drug or approach could have been prescribed after that, without being disclosed on the case report [37].

As for CC05, CC06 and CC07, the system could not recommend radical ADT as a viable treatment option, since, by the guidelines, radical ADT is only indicated for high and very high patients with life expectancy inferior to 6 years and asymptomatic [11,39,46].

For CC08, OnCATs did not suggest the prescribed dose for adjuvant EBRT. Based on the NCCN¬Æ Guidelines for Prostate Cancer, the prescribed dose for adjuvant EBRT after RP should be between 64 and 72 Gy, delivered in

conventional fractionation.[11] For this clinical case, the prescribed dose was 74 Gy. [40] The reasons behind the dose prescription were not discussed on the case report, so it is not possible to assess if this had any relevant clinical advantage.

Lastly, regarding CC10, OnCATs was not able to suggest EBRT with adjuvant BT as a viable treatment option, since this therapy is reserved for intermediate risk patients with life expectancy superior to 9 years and with adverse features [8,11,18,24].

It was apparent that the estimation of life expectancy was the biggest contributor to the accuracy of OnCATs. In 2014, Kent et al. published a study where 14 publications related to models for estimating a prostate cancer patient life expectancy were reviewed [47]. The authors found that most approaches did not consider if the patient had any relevant comorbidities. The simple act of defining to which quartile of health a given patient belongs to, leads to a biased result, since it is only based on a simple subjective analysis. In this study, the method of Kim et al. for calculating the estimated life expectancy for prostate cancer patients was also reviewed. Regarding this method, the authors found its results to be implausible, since they found no reliable connection between the output risk of death by prostate cancer and the patient's age, which is not in concordance with clinical experience. In general, the authors found that even though clinical guidelines include the estimated life expectancy of a patient as a key factor for assessment of the optimal treatment course, no appropriate tool exists to accurately estimate this value, and this may constitute a setback for the development of Clinical DSS tools [47].

V. Conclusions

In general, OnCATs' algorithm showed promising results on recreating the clinical workflow described on guidelines for treatment of localized prostate cancers patients, including valuable steps such as risk group assessment, treatment assessment and treatment prescription.

As for treatment course assessment, we found that the estimation of the patient's life expectancy can highly impact the output generated by the system. Since any optimal methods for estimating to automatically estimate the life expectancy of a prostate cancer patient were not found, new methods should be investigated and researched in the future. This study also allowed the comprehension of the workflow to which a cancer patient is put through when diagnosed with a tumor and its translation to a software meant to assist healthcare professionals on performing medical tasks.

Regardless of the results obtained by applying clinical cases to the systems, it is important to mention that most prostate cancer patients have multiple treatment options and different prescriptions. This translates to different physicians being able to choose different courses of action for the same patient, while applying different prescriptions, based on their experience and judgment, without compromising the patient's outcomes and quality of life.

The incorporation of a decision support system to aid healthcare professionals is of major importance for acting but also for training.

Appendixes

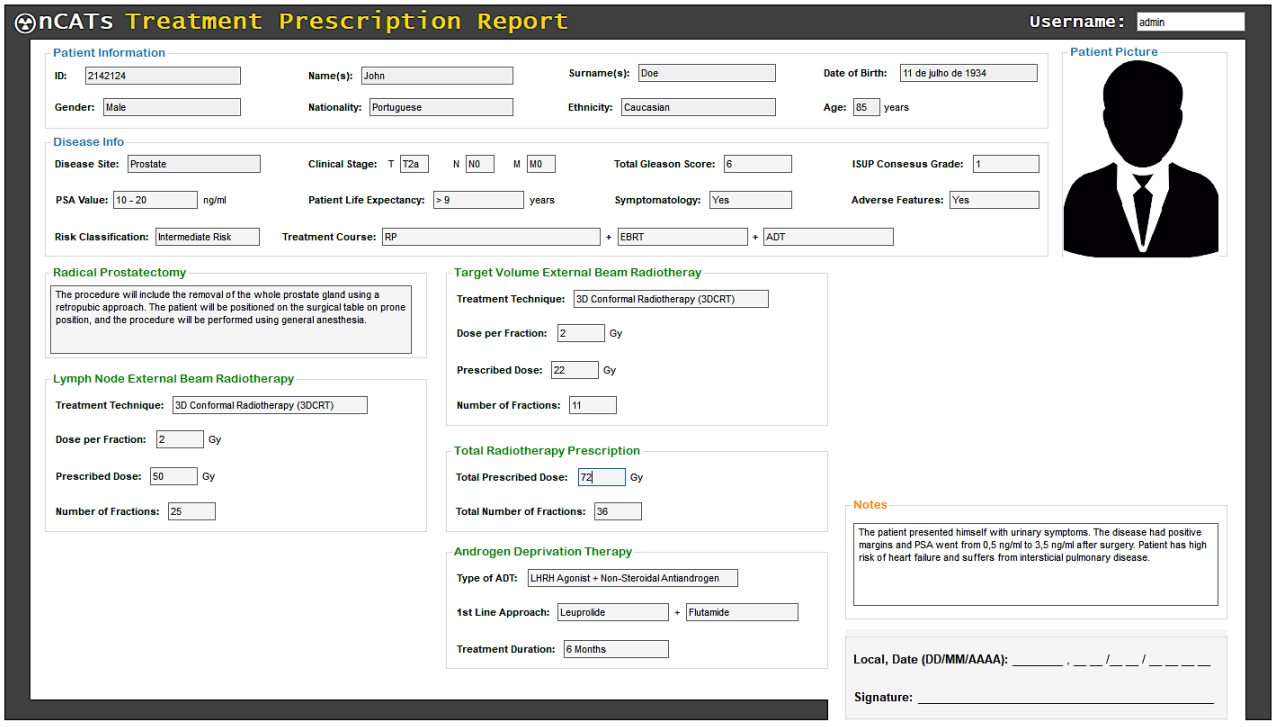

Fig. 2 Example of a final report generated by OnCATs for a patient who underwent RP with adjuvant EBRT and ADT

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