In Silico clinical trial in lung, prostate and head&neck cancer, comparing photons, protons and C-ion therapy treatment: a multicentric planning study based on a reference dataset of patients: Evaluation of feasibility

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Introduction

The In Silico trial investigates whether , with the same dose on the tumor, particle therapy decreases irradiation of normal tissue and therefore decreases the risk of both side effects and of secondary tumor induction. The trial will investigate 3 tumor indications: head and neck, prostate and lung cancer tumors. The expected outcome of the study is to identify (sub) groups of patients who might benefit from particle therapy. the new name of the project is **ROCOCO. It** stands for ***R**adiation **O**ncology **CO**llaborative **Co**mparison* project. . **In this work**, the “In silico trial” is introduced and issues related to initiating an international research study in the field of treatment planning comparisons are discussed.

Fig. 1 *South side - The **Catherine Palace** is the Rococo summer residence of the Russian tsars.* ***Here,*** ROCOCO stands for *Radiation Oncology COllaborative Comparison* Project.

Materials & Methods

Photon, proton and 12C-ions curative radiotherapy plans are performed using the same “state of the art” images and structure delineations, dose specifications, dose constraints and fractionation schedules. To prevent for patient selection, patients are consecutive included in this trial. Treatment plans are compared based on NTCP of OAR. The cooperating centers are MAASTRO, DKFZ, MGH, UMCG, UHG, NKI, PSI, NIRS, CPO, UK Aachen. MAASTRO,UMCG and UHG will supply patient data and MAASTRO acts as data host and coordinator. The photon, proton and C-ion TP for H&N will be performed in UMCG, PSI and DKFZ, respectively. For lung, it will be performed by NKI, MGH and NIRS. For prostate, it will be performed by UHG, MGH and DKFZ. The project is defined by a protocol which describes the patient data, defines the criteria for treatment planning and sets the tasks to the participants. Issues related to initiating the project were scientific, technical and managerial.

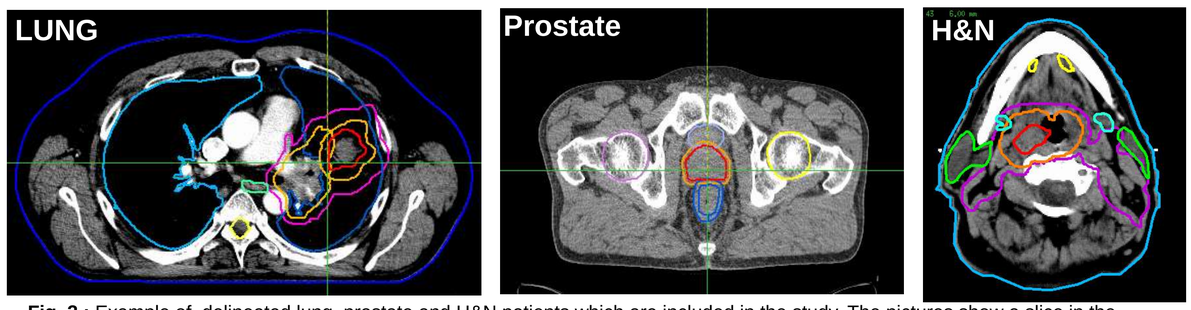

Fig. 3 : Example of delineated lung, prostate and H&N patients which are included in the study. The pictures show a slice in the transversal plane with contours of the volumes of interest the including the GTV (red) CTV (orange), PTV (purple) and primary organs at risk (green, blue and yellow). Patient data from MAASTRO, UHG and UMCG, respectively.

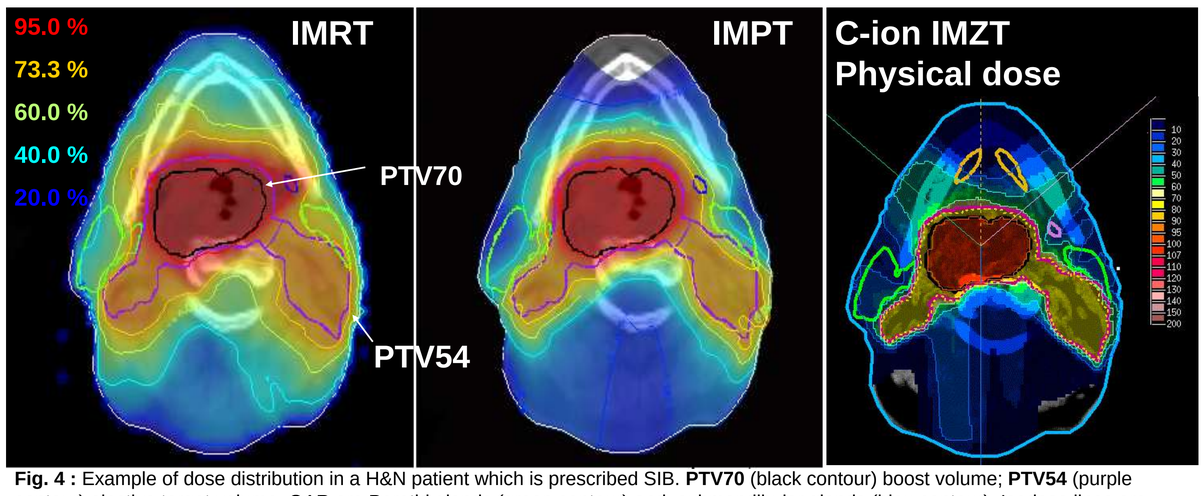

Fig. 4 : Example of dose distribution in a H&N patient which is prescribed SIB. **PTV70** (black contour) boost volume; **PTV54** (purple contour) elective target volume, OAR are Parotid glands (green contour) and submandibular glands (bleu contour). Isodose lines are specified in % of the prescribed dose to PTV70, 70Gy (73.3% isodose line specifies 95% of the prescribed dose to PTV54, 54Gy). IMRT and IMPT dose plans from UMCG, PSI and DKFZ, respectively .

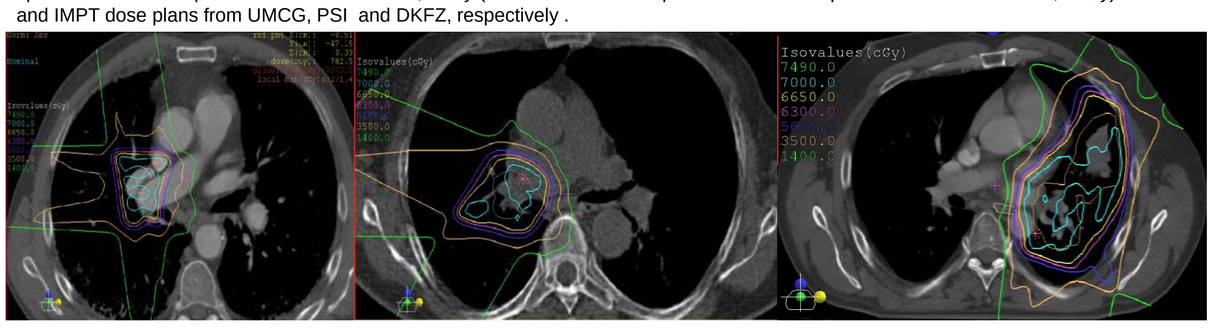

Fig. 5 : Example of dose distribution of Protons calculated in three different patients. The isodose levels shown are, respectively 100, 95, 80, 50 and 20%. Dose plans from (MGH.

3 Tumor Indications

Lung, prostate and H&N

X 3 Modalities

Photon, Proton, C-ion

X 25 Patients

Fig. 6 : in the project layout, 3 tumor indications will be considered. 3 modalities of treatment plans including photon, protons and C-ions will be considered for 25 patients. At least 225 treatment plans will be performed by 10 centers world wide

Results

Most issues addressed while initiating the project were settled by in the project protocol. The participants agreed on treatment planning criteria, NTCP models, criteria for interpretation of motion, and toxicity scoring systems. Insuring the scientific integrity of the project was by incorporating centers with longstanding experience in particle and/or photon radiotherapy and requesting endorsements by PTCOG, EORTC and ESTRO. For comparison of treatment plans , each patient is considered his /her own control,. Biologically effective dose will be compared based on the NTCP models of the OAR. Technical issues related to data export and import, access to the data, compatibility of different treatment planning systems which are used by the centers, tasks of the participants (resources) seem to be overcome. Data transfer and access is regulated via a secured FTP site. At least one member of the participating centers has access to FTP site. For data export and import, DIcom is used for images and DIcom RT for dose plans. A unified MatLab platform will be used to analyze the results from the different centers. Technical issues were addressed during a dummy run of the project for a selected number of patients for each indication. Preliminary results of a H&N case and several lung cases are shown in figure 3 and 4. The management of information flow were controlled through regular communication channels (including the ftp site) and twice yearly review meetings are set to ensure project progress, to discuss results and to implement new insights regarding patient selection and data analysis. The work flow is evaluated monthly using BSC . Finally, Authorship rights were resolved by agreeing on Material Transfer agreements (MTA).

Conclusion

The multi-centric In-silico clinical treatment planning study seems to be feasible. Endorsements by ESTRO, EORTC and PTCOG is underway. The results of the study can be used to negotiate the benefits of particle therapy with national health authorities. A second review meeting is set in September 2008 where results will be shown and evaluated.