

# Clinical trials projects in SSRT

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**Keywords:** Clinical trial, human patients, stereotactic radiotherapy, synchrotron radiation, photo-electric effect, brain tumors.

## Introduction

Heavy-atom-enhanced synchrotron stereo tactic radiotherapy (SSR) is a treatment that involves loading of high-Z elements in tumors followed by stereotactic irradiation. Tomotherapy mode or equivalent is applied with monochromatic X-rays from a synchrotron source, tuned at an optimal energy to obtain an enhanced absorption in loaded tissues. The irradiation geometry, as well as the fluorescent X-rays, the photoelectrons, and some Auger electrons generated by high-Z atoms by synchrotron X-rays produce a localized dose enhancement. Two complementary SSR approaches have been developed in vitro and on animals model at ESRF by the INSERM U836 team 6, that have been authorized to be translated into clinical phase I-II trial with brain metastasis as first human model.

## Materials and Methods

The preparation of a clinical trial is in progress. The medical objectives have been defined by the medical team of brain tumors, neuroradiology and radiotherapy of Grenoble University Hospital in close collaboration with the scientific teams of ESRF (ID17) and INSERM U836/E6. After a stabilized clinical design the technical requirements have been established with the technical and engineering teams of ESRF. After administrative and financial clearance, technical transformations and material development have been designed on the bio-medical beam line ID17. Then a careful description of each elementary step, in both participating institutions CHU and ESRF, has been initiated to build the thorough schedule of the clinical trial. Meanwhile the progress of the protocol through the medico-administrative process of approbation continues with the crucial support of the Centre for Clinical Investigation of the CHU.

## Results

A multi-step comprehensive study has been designed. The main objective is the tolerance and the harmlessness of the SSRT; tumor response and survival feature will be only secondary objectives. The type of tumors chosen for this first trial will be brain metastases in low number 1-3 and of small size 1-3 cm supra tentorial, uptaking iodine contrast agent, in patients requiring brain radiotherapy with complementary boost as the standard of care. Step 0: will test the treatment planning system, the imaging, the contrast injection and repositioning devices without real treatment; Step 1: will test rising dose of SSRT as a progressive substitution of the local boost of a brain metastasis treatment with i.v. injection of iodine contrast. The starting dose will be 5 Gy in one session; the target dose is 10 Gy in one session. Step 2: will be a complementary dose escalation step with iodine dose escalation and introduction of fractionated SSRT the target will be to obtain iodine

concentration above 5 mg/ml in the tumor, target being 10 mg/ml; the target SSRT dose is 24 Gy in three weekly sessions. Step 3: is design to introduce platinum compounds and Step 4 is optional and foreseen to optimize the platinum administration method according to the present state of the art at the time of step 3; it could be the introduction of convection enhancement delivery by direct injection in the tumor tissue. Each successive level of the protocol along the different steps will involve at least 3 patients. A calculation of the decrease confidence interval of risk of the main complication that could be expected will be performed along the accrual process. About 43 to 45 patients will be needed to complete this trial.

## **Conclusions**

As a phase I-II trial, anti-tumor results are not the principal goal. Many other trials will be needed to approach real anti-cancer concerns and to tentatively define appropriate indications. In fact, the present objective is to allow human patient to enter clinical trials with synchrotron radiation and to build a standard procedure to implement new ideas and concept to test with a demonstrated and feasible procedure with patient instead of “far from the clinic” animal models with no real future.

## **References**

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