Internal gold fiducials placement before Cyberknife treatment: how to be of real help for the radiotherapist?

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Authors: B. Richioud, A. Zioueche, M. Cuinet, L. Claude, P. Thiesse; Lyon/FR
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Purpose

Stereotactic Body Radiation Therapy (SBRT) usually delivers high dose radiation in few fraction. Cyberknife (CK) system requires a mechanism to track the lesions to ensure submillimetre accuracy and safety. In particular, gold fiducial are necessary for liver and adrenal lesions, because they move with the breath.

According to the literature data, the liver mainly moves in a superior/inferior direction (mean 16.7mm, range [10-25]) but also in a antero/posterior (mean 7.1mm, range [6-8]) and in a lateral directions (mean 5.5mm, range [2-9]) [1-8]. Adrenal glands also moves with the kidney during the breathing cycle, principally in superior/inferior way (mean 11.4mm, range [8.8-15.3]), but also in lateral direction (mean 2.75mm, range [2.5-3]) and antero/posterior directions (mean 5mm, range [3.2-7.6]) [1,2,6,7].

As a consequence the best way to proceed is probably to follow the tumor movement during the breathing cycle. thus, gold fiducials implanted in or around the tumor can be efficiently tracked for the Cyberknife using Synchrony system®.

To be efficiently tracked, fiducial implantation requires answering different critera. One fiducial is enough to correct translations, while at least 3 fiducials are necessary to correct both translations and rotations.

Markers are placed near and surrounding the tumour but not inside the target to avoid a spread of tumour cells [9-11]. However, Seppenwoolde et al. showed that marker-guided set up accuracy decreased with an increasing distance between implanted markers and the tumour [11].

Ideally, the distance between markers should be over 20mm to recognize them. The minimal angle between them should be over 15° [12]. Fiducials have to be visible on two 45° angles radiographs for tracking and should be positioned within 4cm of the lesion [11].

These rules seem to be simple but in pratice, the number of fiducials effectively tracked is usually under thre, leading to a poorer treatment quality than it could be.

The goal of this study is to report our experience in fiducials placement and tracking for liver and adrenal gland tumors. The efficiency of the fiducials placement is assessed thanks to a "score of satisfaction" according to both radiotherapist and radiologist. We try to identify the causes of the misfits, in order to improve the quality of the fiducials placement and as a consequence, the CK tracking.

Methods and Materials
Study population

Twenty patients treated using CK for hepatic (n=14) or adrenal (n=6) malignant lesions at the Centre Leon Berard, France, from 10/2010 to 12/2011 were retrospectively reviewed.

Fourteen patients had a liver lesion. Two of them were treated for a primary liver lesion (14%) and 12 for a secondary lesion (86%). Among them, 7 patients (50%) had a primary colorectal cancer, 4 patients (29%) a primary lung cancer, and one patient (7%) a primary breast cancer.

All the 6 patients with adrenal gland lesions were treated for metastasis. Three patients (50%) had a primary lung cancer and 3 patients (50%) a primary kidney cancer.

Fiducial placement procedure

Fiducials are metal markers placed in the body to be tracked with the CK system (Fig. 1). They are composed with almost pure gold and are radiographically visualised by kilovoltage X-Rays. They are supplied in sterile bags. Two types of fiducials were used during the period of our study: sterile (1 x 5mm) CyberMark Marker® and sterile placement needle (17 gauge needles x 20cm) with (1 x 3mm) coupled marker®. In our institution, image-guided percutaneous procedures were performed by two interventional radiologists, under local anesthesia in every case, helped by hypno-analgesia in two cases (10%).

At the beginning of CK activity, both radiologists learned how to implant the fiducials according to Accuracy® recommendatons:

- minimal number of fiducials = 3
- minimal distance between two fiducials = 20mm
- minimal angle between fiducials = 15°
- maximal distance between fiducial and tumour = 5cm

Radiotherapy procedure

CT dosimetric scan (DCT) was performed more than 7 days after the fiducials placement, and less than 7 days before the radiation therapy, to reduce the risk of migration between DCT and CK treatment.

During the therapy on the treating table, two 45°- angled radiographs were obtained centering the beam at the lesion every few seconds, to track the tumour according to the patients movements (Fig. 2-3).
Efficiency of the fiducials placement

The radiologist determined a "score of satisfaction" according to the criteria defined above. This score reflected the number of fiducials he thought possible to be tracked after the fiducials placement: 0 for 0 fiducial, 1 for 1 or 2 fiducials, and 2 for 3 fiducials.

The radiotherapist determined independently the same score of satisfaction based on the number of fiducials really tracked during the CK treatment.

Images for this section:

Fig. 1: Internal gold fiducials: aspect and spatial representation around the tumour.
Fig. 2: Cyberknife and treating table
**Fig. 3:** Two 45°-angled radiographs are obtained during the treatment every few seconds, to track the fiducials
Results

Fiducials placement and complications

Between September/2010 and September/2011, seventy-two fiducials were implanted in 20 patients with a median of 4 [range 3-5] fiducials per patient, using a percutaneous procedure. Local anesthesia was used in every patients, helped by hypno-analgesia in two cases. A normal coagulation was required before implantation. The implantation was CT-guided for 9 patients (45%), Ultra-Sound (US)-guided for 5 patients (25%) and both CT scan and US-guided for 6 patients (30%). At the end of the procedure for each patient, the quality of implantation was controlled by a CT scan.

Patients remained in bed under observation for one night. The main frequent acute complication was pneumothorax in 4 patients (20%) without need of drain. One patient (5%) developed a supra-capsular hematoma requiring the use of intravenous medication (level 2). No severe late complication (level # 3 CTC-V3) was reported after fiducial placement.

A migration of one fiducial was observed in two cases (one patient with adrenal gland lesion and one with a liver tumour).

Score of satisfaction

The radiologist satisfaction score was 0 in 5 patients (25%), 1 in 7 patients (35%) and 2 in 8 patients (40%).

The radiotherapist satisfaction score was 0 in 1 patient (5%), 1 in 10 patients (50%) and 2 in 9 patients (45%).

The radiologist and the radiotherapist obtained the same score in 12 patients (60%) as shown in Table 1. Among them, 1 lesion (5%) was tracked on 1 or 2 markers, and 6 lesions (30%) were tracked on 3 markers or more.

On the eleven patients with tracking using less than 3 fiducials, several reasons were identified by the radiotherapist at the time of treatment: proximity of the fiducials (n=3, 28%), coplanar characteristics (n=1, 9%), both proximity and coplanar characteristics (n=5, 45%), migration of fiducials (n=1, 9%), and both migration and proximity of fiducials (n=1, 9%). Among them, the radiologist was able to identify in 7 cases (63%) at least one of the causes of tracking problem.

Images for this section:
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**Table 1:** Correlation between radiologist and radiotherapist scores of satisfaction.
Conclusion

Fiducials are necessary to track liver and adrenal lesions during stereotactic radiation treatment using Cyberknife®. Our study confirms that image-guided placement is a safe procedure if performed by experimented radiologists. We report 25% of acute toxicity grade 1-2 without toxicity # grade 3 after fiducial placement. The most frequent side effect was pneumothorax resolving spontaneously, followed by pain and hematoma. The literature reports also high rates of accuracy and little toxicity concerning fiducial implantation. Mallarajapatna et al. reported the results of 450 fiducials implanted in the chest, abdomen or pelvis, performed by percutaneous procedures, under local anesthesia. They reported one significant pneumothorax for wich a chest tube was inserted and two moderate hemothorax which did not require specific treatment [12]. Sotiropolou et al. described their large experience in a retrospective study on 105 patients. A total of 319 gold fiducials were implanted. Again, little toxicity was reported : one pneumothorax requiring drainage, one mild pneumothorax and 3 focal pulmonary haemorrhages [13]. The acute toxicity we report is acceptable but slightly higher, probably due to a learning curve, while the current results reflect the beginning of the CK use.

To our knowledge, this study trying to quantify and identify the different reasons of difficulties for fiducial tracking in liver/adrenal gland is the first one. Ideally, 3 fiducials are necessary at least to correct both translations and rotations. However, 3 fiducials or more could be tracked during CK treatment in less than 50% of the patients, so the radiologists tried to improve their technic by meeting and discussing with the radiotherapists :

- Radilologists initially tried to place every fiducials within the tumour. this led to close fiducials, poorly individualized for tracking. The procedure was thus modified : coupled-fiducials are now used instead of single markers, to ensure a sufficient distance between the markers (20mm between two coupled-markers). In addition, radiologists do not place more than one marker directly within the tumour yet.

- Patient’s position during fiducial placement differs from the patient’s position during CK treatment (two 45° angled radiographs) (Fig.4-5). This is highly difficult for the radiologist to avoid coplanar markers while they cannot see the fiducials on two 45° radiographs during the placement procedure (axial slices by CT scan). There is probably a need to develop software able to provide quickly to the radiologist a reconstructed picture of the fiducial position considering two 45° angled radiographs, during the procedure of placement itself. A new procedure has taken place in our institution to avoid coplanar markers : after the third fiducial has been implanted, two images are reconstructed (with 45° angle) from the CT post-treatment, to help the radiologist implanting a 4th fiducial in a right non-coplanar way.

- Considering these difficulties and the time needed to implant correctly the markers, general anesthesia instead of local anesthesia is now scheduled for every procedures. It
is painless for the patients and also gives both more time and comfort to the radiologist. During general anesthesia, an apnea can be maintained for a few seconds, leading to an easier fiducial placement by the radiologist, who is as a consequence more likely to respect "the state of the art" in term of fiducial placement.

This study underlines the need of collaboration between radiologists and radiotherapists. New procedures during fiducials placement have been decided to improve these results since this time, which seems to be helpful for the radiotherapists. We plan now to evaluate them.

**Images for this section:**

**Fig. 4:** Exemple of good fiducials placement : 3 fiducials tracked by CK (surrounded by green)
**Fig. 5:** Exemple of poor fiducials placement: no fiducial could be tracked while they were too close and coplanar. The patient was treated using spine tracking.
References


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