Setup Optimization in Ocular Proton Therapy at the National Centre for Oncological Hadrontherapy: Comparison of Two Approaches to Refine the Position of an Eye-Tracking Device

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Abstract: This study describes a method for setup optimization in patient simulation for ocular proton therapy (OPT) at the National Center for Oncological Hadrontherapy (CNAO) in Pavia, Italy, with the aim of minimizing the occupancy time of clinical areas and streamlining the actual procedure. Setup repeatability is ensured by patient-specific immobilization tools and relies on the patient’s ability to maintain a stable gaze direction according to the treatment plan. This is facilitated by aligning a light source (LED) on a patient-specific base along the prescribed gaze direction. At CNAO, a dedicated Eye-Tracking System (ETS) was designed to provide the patient with a visible source of light aligned to the desired gaze direction. The ETS position is defined prior to treatment planning, relying on optical-tracking guidance and comparing the position of passive markers fixed on the ETS chassis with patient-specific models prepared offline in accordance with the desired geometry. OPT at CNAO started in 2016 and may be considered as a consolidated clinical routine. However, all the preparation phases, including patient-specific ETS models and setup, still require long sessions in clinical areas such as the computed tomography (CT) and the treatment rooms, with a non-negligible impact on other activities. This study describes a novel approach for patient-specific definition of the ETS position and orientation, aiming at minimizing the time required for preparatory activities inside clinical areas. To minimize the occurrence of biases and to reproduce as much as possible a real end-to-end approach, we included in the analysis data of patients that received OPT in our facility. The study was performed in parallel, carrying out the alignment with the standard method currently used in the clinical workflow of CNAO and with the proposed method. Results are presented as 3D residuals and gaze deviations, comparing ETS alignment based on the new approach with respect to the clinical standard method. The preliminary results of this study are evidence of the capability of the procedure to align the ETS position, allowing performing of the procedure in a non-clinical dedicated room.

Keywords: radiation oncology; particle therapy; ocular proton therapy; setup
1. Introduction

Ocular tumors are rare malignancies that can lead to problems with vision, quality of life and life expectancy. Nowadays, the first treatment option is radiotherapy, with enucleation foreseen only for patients with advanced disease [1–5]. Proton beam radiation is well established as the gold standard treatment for ocular melanoma (OM), the most common primary adult eye cancer [1–11].

To define the target volume and to ensure repeatable proper alignment of the eye and the tumor, OPT requires an invasive surgical procedure to implant radiopaque tantalum clips on the surface of the globe near the tumor site [12–15].

In OPT, the repeatability of the setup is guaranteed by patient-specific immobilization tools and by relying on the capability of patients to maintain a steady gaze direction according to the treatment plan. The patient actively participates in the treatment procedure by staring at a fixation light to reproduce the optimal gaze direction (polar and azimuthal angles) planned during setting, as a way to minimize dose to critical structures and achieve full coverage of the target [16–18]. At the time of treatment, the quality of the geometrical setup is verified and iteratively corrected using radiographic images. Furthermore, the reproducibility of the gaze direction is also monitored by dedicated video cameras [18].

At the National Center for Oncological Hadrontherapy (CNAO, Pavia, Italy), OPT treatment started in August 2016 using a dedicated treatment planning system combined with a non-dedicated beam line [18,19].

The clinical workflow envisages the use of a dedicated ocular proton planning software (Eclipse, ver. 13.5.01, Varian medical system) containing a geometric model of the patient’s eye and the position of the lesion, for the definition of the patient-specific gaze direction (polar and azimuthal angles) to optimally align the lesion mass to the beam. At CNAO, the gaze alignment is obtained by using a dedicated ETS device (Figure 1), which accomplishes the dual purpose of assisting the patient fixation and monitoring the eye during treatment by means of an infrared camera embedded in the device [18].

Figure 1. The ETS device provides the fixation light for the stabilization of the patient gaze direction. The external marker geometry permits an accurate positioning of the fixation light using industrial robots and optical-tracking systems. The ETS monitors involuntary eye motion by means of a stereo-camera system embedded in the same device, providing real-time optical imaging of the eye surface.

The first prototype of this device was described in Fassi et al. [20], which reported the hardware and software development of the first prototype of a non-invasive 3D ocular-tracking system designed for the eye localization and for ocular movement detection.
Via et al. [21] developed in 2015 an ETS designed for real time 3D target localization and ocular movement detection, and they described the first clinical trial of the device. With respect to the previous ETS generation [20], the device described by Via and Colleagues ensured full compatibility with CT scan and therapeutic dose delivery, providing minimal space requirements near the eye region. The device provides an aid for the patient to maintain a stable gaze along the planned direction, thanks to the presence of a fixation light that is visible through a reflecting mirror. It also monitors involuntary eye motion by means of a stereo camera embedded in the same device [21].

The alignment of the ETS is a particularly critical task since it has to fulfil the requirement of fixation light correct positioning in the treatment room space and avoiding collisions with the collimator, with the patient and with all other systems in the treatment room. The ETS alignment method proposed by Via et al. [21] suggests an initial device positioning and allows further setup optimization by manual modifications of the ETS position. Elisei et al. [18] described in 2021 the development and commissioning of a software application to optimize the ETS positioning and to overcome the time demanding process proposed by Via and collaborators [21].

The latest development was focused on the use of a robotic manipulator (Mitsubishi Industrial Robot model RV-2F-D, Mitsubishi Electric Europe, Agrate Brianza, Italy) for the definition and successive repetition at each irradiation session of the patient-specific position and orientation of the ETS [18].

An infrared optical-tracking system (OTS) is used to track the position of radio-opaque reflective spherical markers (BrainLab, 1 cm diameter) on the ETS surface and to compare these markers’ positions to the reference configuration generated using the application developed by Elisei and Colleagues [18].

Currently, the ETS alignment procedure takes place twice in clinical rooms, namely the CT bunker and the treatment room, with non-negligible impact in terms of room occupancy. Therefore, the need to standardize and streamline the workflow in order to reduce the time spent in clinical rooms is emerging with particular importance.

The aim of this work is to present an alternative method for ETS alignment out of the CT bunker and to compare the results achieved with the two procedures (the conventional procedure in the CT room and the method proposed in this study). Furthermore, in this study, we focused on finding a solution to overcome the limitations highlighted in previous studies, such as in Elisei et al. [18], and related to the need to exclude from treatment patients for whom a low external gaze direction was required, due to the unfeasibility of the ETS configuration.

Our study includes a wider and more heterogeneous clinical dataset than the one described in Elisei et al. [18], including configurations that required the use of a specific extender attached to the robotic manipulator, in order to reach the planned position.

In the proposed study, the initial alignment of the ETS device in the CT bunker (Figure 2b) was replaced by a corresponding procedure, performed in a dedicated room and supported by a commercial general purpose optical-tracking system (Smart-DX motion analysis system, BTS Bioengineering, Italy) (Figure 2c,d). The position of the three cameras equipping the system was optimized to ensure the optimal visibility of the markers mounted on the ETS chassis and used to localize the ETS critical components (fixation light, monitoring cameras, etc.).

The study focused on the quantitative assessment, in controlled conditions and exploiting retrospective clinical data, of eventual deviations in the ETS setup between the conventional CT bunker-based procedure and the novel one, as the initial step for proposing a change in the clinical procedure with consequent lower occupancy of the CT bunker.
Figure 2. Elements for ETS alignment in the CT room: the OTS-CT, in blue (a), and setup in the CT bunker (b). Elements for ETS alignment in a dedicated room: Smart-DX motion analysis system equipped with three cameras (c) and setup optimized in the laboratory (d).

2. Materials and Methods

2.1. Clinical Workflow

The clinical procedure for OPT at the CNAO consists of two phases: a treatment simulation performed in the CT room with the patient immobilized in the supine position (Figure 2b) and an irradiation phase that takes place in the therapy bunker with the patient in a sitting position (Figure 3). The ETS is used in both phases, and the stream of frames acquired in real time by the stereo cameras is processed through a proprietary custom software aimed at monitoring any involuntary eye motion. The ETS provides also an aid in maintaining the gaze stability by means of a source of light (a red LED) enclosed in the rigid chassis. As the eye bulb is reflected by the mirror and seen by the cameras, the patient can see the reflection of the LED. As a consequence, the relative position of the ETS in reference to the isocenter can be used to uniquely define the gaze direction. The ETS position is refined during setup preparation, on a patient-specific basis. The adopted strategy foresees the minimization of 3D displacements between the ETS position in space and a nominal model. This operation is performed via a point-based rigid registration of surrogates, represented in this case by spherical markers placed in a predefined configuration on the ETS. During clinical routine, 3D coordinates of markers are calculated with optical-tracking systems. For safety reasons we adopt two different sets of markers: made of aluminum and thus radiopaque during CT acquisitions; made of plastic during treatment.
In order to highlight the impact that the explored novel procedure could have in the clinical workflow of OPT at CNAO, we report the essential steps of the currently adopted procedure. It is worth recalling that, in order to localize the malignant lesion inside the eye, a set of radiopaque fiducial clips are sutured around the lesion during a preliminary surgical intervention and used as tumor localization surrogates for treatment planning and patient setup. At CNAO, the treatment plan is elaborated by means of a dedicated software (Eclipse, ver. 13.5.01, Varian medical systems, Palo Alto, CA, USA), which outputs the optimal geometrical solution to focus the dose on the target, while sparing radiosensitive healthy structures within the eye. The main geometrical parameters optimized by the treatment planning system are the gaze direction angles (expressed in polar coordinates) required to expose the tumor mass to the delivered horizontal proton beam. Patient cooperation is required to maintain the planned gaze direction during irradiation, and proper verification is needed to ensure setup stability at all phases of the irradiation session.

In particular, the treatment simulation consists of three main steps:

1. Planning CT scan (CT0): The patient is fitted with the immobilization thermoplastic mask and undergoes a first CT scan of the diseased eye while keeping the gaze straight ahead (Figure 4). Proper sight direction is ensured by a corresponding positioning of the ETS and ocular motions are detected through the video stream coming from the two stereo-cameras embedded in the ETS. The manual contouring of the iris and pupil on the ETS PC monitor serves as reference for the qualitative detection of ocular motion.

2. Gaze direction and model generation: On the CT0, the treatment plan is elaborated, and the deviated optimal gaze direction provided by the treatment planning software is translated into a corresponding ETS position and orientation expressed in terms of reference coordinates of the radiopaque, retroreflective markers attached to the ETS case [18]. This allows the OTS installed in the CT bunker to guide the robotic manipulator through a recursive process until the position deviations between the current and reference marker positions on the ETS are minimized ($\leq 1$ mm, $\leq 1^\circ$), thus ensuring the correct definition of the fixation light position and consequently the prescribed deviated gaze direction within the CT bunker space.

3. Verification CT scan: In order to verify the obtained geometry and acquire the data necessary for the patient alignment in the therapy bunker, a second CT scan is performed while the patient is asked to stare at the fixation light within the ETS, which is preliminarily positioned as described in the previous step, thus aligning the gaze along the prescribed direction (Figure 5). Also at this stage, the iris and pupil profiles are manually contoured on the ETS PC monitor to control gaze stability.
Figure 4. The ETS position used for CT0 planning image acquisition is shown. The fixation point is projected along the patient’s straight-forward gaze direction.

Figure 5. Optimization of ETS positioning for the verification CT scan using the software application available in the clinic. In (a), the green dotted line represents the gaze direction; the blue dots are a virtualization of the markers; the blue area on the ocular region of the patient depicts the FoV projection of the ETS on the mask. In (b), the patient gaze is directed towards the fixation light reflected on the mirror. An example is shown with polar 28° and azimuth 90° (b).

2.2. ETS Alignment

Since CT0 and verification scans take place on different days, it is worth underlining that the main aim of this study was to avoid performing step #2 (ETS alignment) within the CT bunker, taking advantage of a more flexible optical-tracking configuration in a dedicated non-clinical area (Figure 2c,d).

A schematic representation of the new workflow proposed in this study is depicted in Figure 6.

Based on the optimal gaze direction provided by the treatment planning software, the ETS reference configurations were generated in Matlab (The Mathworks, Inc, Natick, MA, USA), as described by Elisei [18].

The experimental setup was meticulously prepared to ensure optimal reproducibility and precision to align the ETS. As described in Figure 6, this involved: (1) Proper orientation of three near-infrared cameras to optimize visibility of the ETS handling area. (2) Optimization of camera parameters (focus, zoom, diaphragm aperture) to enhance calibration outcome and minimize residuals.
2.2. ETS Alignment

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A schematic representation of the new workflow proposed in this study is depicted in Figure 6.

**Figure 6.** Workflow scheme—setup preparation and ETS position alignment with proposed method. Differences (highlighted in red box) between the current method in setup preparation and the use of a different OTS. To verify the accuracy between the two results, CT acquisition was performed to extract the coordinates of the center of radiopaque markers on the ETS surface for both configurations (standard method and proposed method).

OTS features the 3D localization of passive, reflective markers through real-time processing and triangulation of the image data coming from the cameras [22,23].

OTS optical calibration was performed using a wand-based method to estimate both intrinsic and extrinsic camera parameters. The calibration process was divided into two stages: static and dynamic. The static phase is performed by means of an orthogonal set of wands to establish a spatial coordinate system. In the dynamic stage, a single wand with three markers is moved within the calibration volume, to refine camera parameters and ensure comprehensive 3D motion-tracking coverage [24–26].

The required mapping among the native OTS reference system, with respect to which the 3D coordinates of the markers are reconstructed, and the CT/patient reference system were obtained by acquiring the ETS-mounted markers’ positions after driving the robotic manipulator in the same configuration used for CT0 acquisition. As a result, the corrections estimated through optical tracking are executed by the robotic systems in a geometrically consistent way. Corrections of the ETS position are estimated from a point-based rigid registration between the current ETS fiducial configuration measured in real-time by OTS and a pre-defined geometrical reference.

As already described (step 2 of the clinical treatment simulation workflow), the ETS alignment is performed by driving the robotic manipulator until the misalignment between the current ETS-mounted markers and the reference position detected by the OTS is mini-
mized (Figure 7). The OTS detects the position of the ETS markers in real time and provides motion correction parameters (6 degrees of freedom (DOF)) for accurate alignment of the actual configuration against a predefined reference and indirectly of the fixation point to minimize misalignment between the ETS-mounted markers and the reference position detected by the OTS.

In this study, for each of the examined cases (see Section 2.3, Dataset) we performed the procedure illustrated in Figure 6 in the dedicated laboratory and in the CT bunker (according to the standard clinical routine). This dual-environment approach was designed to mimic a realistic clinical approach. The procedure resulted in two distinct configurations of the ETS. To compare these configurations, we performed CT scans of the ETS device itself in each configuration with an axial resolution of 2 mm.

For comparison, we extracted the coordinates of radiopaque marker centers using a software available at the CNAO [18], and we evaluated the distance between corresponding markers in the two ETS configurations.

Moreover, for a more clinically meaningful comparison, the polar coordinates of the fixation light embedded in the ETS system were extracted under the two configurations and directly compared.

These comparisons gave us a detailed understanding of the accuracy and precision of the method in terms of reproducibility of the markers’ positions and the fixation light position. This information is crucial, as accurate and repeatable patient positioning is critical to the success of clinical procedures. Furthermore, the analysis of the polar coordinates of the fixation light provided an additional level of comparison directly relevant to clinical practice, as the position of this light is a key indicator of patient positioning.

2.3. Dataset

For this study, the clinical data of forty patients, nine treated in CNAO and thirty-one clinical-like patients generated for data augmentation by simulating different gaze configurations, were considered.

Patients with ocular melanoma in both the right and left eyes were included and the gaze angles were chosen to consider different configurations.

Table 1 shows the planned gaze angles for the real patients included in the study. In order to augment the available data, the clinical dataset was increased by simulating further
cases of clinical-like planned gaze angles, giving rise to a more statistically robust dataset of cases for comparing the ETS alignment performed in the CT bunker and in the dedicated non-clinical laboratory.

**Table 1.** Fixation angles of the patients treated at CNAO considered in the study. Left eye (L) and right eye (R).

<table>
<thead>
<tr>
<th>Diseased Eye</th>
<th>Fixation Eye</th>
<th>Polar [°]</th>
<th>Azimuth [°]</th>
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As described in Section 2.1 (step #1), during the simulation phase a patient-specific thermoplastic mask is generated prior to the straight-look CT scan (CT0). At this stage, the patient’s diseased eye is carefully aligned with the isocenter of the CT gantry using the room lasers and geometric references are marked on the mask accordingly. In the context of our research, we randomly collected 9 masks that were used to increase the testing dataset of this study. We created dummy fixation angles (polar and azimuthal) simulating a treatment scenario. In this way, we obtained a more consistent dataset with different fixation points, which allowed us to test the functionality of our method and increase the robustness of our results.

As already mentioned, the comparison was performed by assessing the deviations between the coordinates of corresponding ETS-mounted marker centers in the two ETS configurations.

### 3. Results

The comparison between the positions achieved with the proposed method and the currently applied clinical workflow within the CT bunker is depicted in Figure 8b, which summarizes the positioning of the fixation light extracted from the ETS geometry in cases of OM in the left and right eyes for the nine patients treated in CNAO.

**Figure 8.** Representation of polar and azimuthal angles that identify the fixation point (a). Aligned position of the fixation point of the nine patients treated in CNAO, comparison between clinical results (blue) and the results of the proposed method (Test, in green) (b). All nominal fixation points of the complete dataset (in red, real patients are highlighted) considered in the study (c).
The 3D distance of the corresponding markers in the two ETS configurations (clinical and test) had a median value of 3.33 mm with an interquartile range (IQR) of 2.18 mm. The corresponding deviations on polar and azimuthal gaze angles were $0.37 \pm 1.12^\circ$ (median ± IQR) for the polar angles and $0.32 \pm 1.33^\circ$ for the azimuthal angles.

Figure 9 shows the boxplots that detail the positional deviations affecting the ETS-mounted markers calculated for the clinically applied procedure and the proposed test procedure, with respect to the nominal prescription coming from the treatment plan and the ETS modeling described in Section 2.1 (step #2).

The corresponding median differences in terms of gaze direction were $-1.10^\circ$ (IQR = 1.13°) for the polar angles and $-0.24^\circ$ (IQR = 1.28°) for the azimuthal angles, when the clinical procedure was considered. Conversely, median angular deviations were $-1.47^\circ$ (IQR = 1.09°) for the polar angles and $-0.11^\circ$ (IQR = 0.75°) for the azimuthal angles, when the proposed procedure was applied. The augmented dataset including simulated clinical-like cases is reported in Table 2.

When the deviation analysis was performed on this dataset, we found a median difference of $0.01^\circ$ (IQR = 0.96°) for the polar angles and $-0.32^\circ$ (IQR = 1.47°) for the azimuthal angles between the clinical and test methods. When comparing the clinically applied procedure and the nominal prescriptions, we estimated a median difference of $-1.32^\circ$ (IQR = 1.19°) for the polar angles and $-0.40^\circ$ (IQR = 1.09°) for the azimuthal angles. When the ETS configuration obtained with the proposed method and the nominal prescriptions were compared, a median difference of $-1.33^\circ$ (IQR = 0.91°) for the polar angles and $0.16^\circ$ (IQR = 0.99°) for the azimuthal angles were found.

When less frequent fixation angles were included in the dataset (Table 3), we estimated a median difference of $-0.13^\circ$ (IQR = 0.98°) for the polar angles and $0.16^\circ$ (IQR = 1.75°) for the azimuthal angles between the clinical and test method.
Table 2. Fixation angles of the simulated clinical-like patients considered in the study. Left eye (L) and right eye (R).

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Table 3. Patients with downwards fixation angles. Left eye (L) and right eye (R). One patient used the healthy eye as the fixation eye as he was unable to see the ETS fixation light with the diseased eye.

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Considering the limited population of 40 patients, we applied statistical analysis aimed at investigating potential differences in polar and azimuthal values between Group 1 (difference between polar and azimuthal values obtained by the clinical method and the planned reference values) and Group 2 (difference between polar and azimuthal values obtained by the proposed method and the planned reference values).

Mann–Whitney U test ($\alpha = 0.05$) reported a non-significant difference among the two groups, both for polar and azimuthal angles. All statistical analyses were performed in Matlab (MATLAB and Statistics Toolbox Release R2020b, The Mathworks, Inc, Natick, MA, USA).

In the boxplot analysis (Figure 10), the median (IQR) values for Group 1 were $-1.52^\circ$ (IQR = 1.48°) for polar angles and $-0.28^\circ$ (IQR = 1.28°) for azimuthal angles, and for Group 2 $-1.38^\circ$ (IQR = 1.28°) and $-0.11^\circ$ (IQR = 1.08°) for the polar and azimuthal angles, respectively.
with the planning reference. A clinical operator manually detects the clips' center in the images. For this purpose, before and during irradiation, X-rays are used to verify the correct alignment of the eye by comparing the actual configuration of the tantalum clips around the lesion in CT images. The deviations come from inaccuracies in optical-tracking camera calibration, residuals in reference system mapping and intrinsic accuracy of the robotic manipulator used for ETS alignment. It is worth recalling that the effects of these deviations are checked and eventually compensated for at the time of treatment by a point-based registration between reference and current positions of the implanted fiducial clips around the lesion in CT images. For this purpose, before and during irradiation, X-rays are used to verify the correct alignment of the eye by comparing the actual configuration of the tantalum clips with the planning reference. A clinical operator manually detects the clips' center in the radiographic images and a commercial software (VeriSuite 1.8, Medcom GmbH, 2012)

Figure 10. Boxplot of statistical test for the difference in polar (a) and azimuthal angles (b) between Group 1 and Group 2, including 40 patients. The $p$-value for the rank-sum test indicates that there are no significant differences in the distribution of scores between the two methods.

4. Discussion

In this study, we reported an alternative workflow for OPT in the frame of the specific CNAO case, where a non-dedicated fixed horizontal beamline and an ETS work in synergy for treatment delivery to patients affected by OM. In particular, the investigated modification of the clinical procedure concerned the phase in which the ETS is aligned in order to position the embedded fixation light along the prescribed gaze direction retrieved from the treatment plan. Currently, this procedure is performed inside the CT bunker with the aid of a dedicated in-house developed marker-tracking device [17,18]. We proposed a method envisaging this procedure to be performed in a dedicated non-clinical room equipped with a general purpose infra-red optical-tracking device as a way to limit the occupancy of the CT bunker with not strictly clinical procedures.

For comparing the conventional versus the alternative proposed method, we merged a dataset consisting of the retrospective data coming from patients already treated at CNAO and simulated cases with clinical-like irradiation geometries, and ETS alignment was performed under the two conditions. When aligning the ETS in the dedicated room, certain limitations related to the lower flexibility of the OTS installed in the CT room were overcome by exploiting the more flexible three-TVC configuration of the commercial infrared tracking device.

The comparison gave rise to similar performance in ETS alignment and corresponding gaze direction definition with respect to the nominal prescription under the two investigated conditions.

In general, the residuals (nominal vs calculated) on the polar coordinate were greater than those on the azimuthal coordinate for both methods (clinical and novel). The differences we found were within or slightly higher than the clinical threshold of attention ($1^\circ$), both when the retrospective patient data were considered alone and when the dataset was augmented with simulated cases.

The deviations come from inaccuracies in optical-tracking camera calibration, residuals in reference system mapping and intrinsic accuracy of the robotic manipulator used for ETS alignment. It is worth recalling that the effects of these deviations are checked and eventually compensated for at the time of treatment by a point-based registration between reference and current positions of the implanted fiducial clips around the lesion in CT images. For this purpose, before and during irradiation, X-rays are used to verify the correct alignment of the eye by comparing the actual configuration of the tantalum clips with the planning reference. A clinical operator manually detects the clips' center in the radiographic images and a commercial software (VeriSuite 1.8, Medcom GmbH, 2012)
estimates a correction vector based on the distance between the clips’ center in the nominal configuration and the actual configuration. A three-DOF correction vector is consequently applied to the treatment chair aiming at minimizing setup deviations.

Among the reasons causing the detected deviations, optical-tracking intrinsic accuracy and calibration residuals influencing the overall 3D markers’ localization accuracy are the ones that we consider more relevant. As a matter of fact, Table 4 shows the 3D localization accuracy of calibration residuals of the general purpose OTS used in the laboratory for ETS alignment and of the optical system installed in the CT room (OTS-CT). Data were obtained by localizing a known marker configuration with known coordinates in agreement with the quality assurance (QA) daily procedure adopted at CNAO [27].

Table 4. Calibration residues of Smart-DX system compared to the optical-tracking system residues in the CT room.

<table>
<thead>
<tr>
<th></th>
<th>Pitch [°]</th>
<th>Roll [°]</th>
<th>Yaw [°]</th>
<th>X [mm]</th>
<th>Y [mm]</th>
<th>Z [mm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smart-DX</td>
<td>Mean</td>
<td>0.01</td>
<td>0.06</td>
<td>−0.15</td>
<td>0.18</td>
<td>−0.20</td>
</tr>
<tr>
<td></td>
<td>Std</td>
<td>0.26</td>
<td>0.07</td>
<td>0.17</td>
<td>0.24</td>
<td>0.53</td>
</tr>
<tr>
<td>OTS-CT</td>
<td>Mean</td>
<td>0.01</td>
<td>−0.05</td>
<td>−0.08</td>
<td>0.06</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>Std</td>
<td>0.59</td>
<td>0.26</td>
<td>0.24</td>
<td>0.17</td>
<td>0.33</td>
</tr>
</tbody>
</table>

On average, the calibration residuals of the two optical systems used in the proposed method (Smart-DX) and in clinical practice (OTS-CT) do not differ significantly in terms of accuracy (calibration residuals below 1 mm and 1°).

Also, the two optical systems rely on two different types of tracking: OTS-CT detects markers in the blue range, while OTS detects reflective markers; the diameter of the two different markers was characterized using a Laser Tracker system (Leica AT960-MR, Hexagon) and we verified that there were no significant diameter differences (diameter median difference value (interquartile range) is 0.07 (0.11) mm).

Nevertheless, the results of this study show that ETS alignment outside of the CT bunker is feasible with no or negligible difference with respect to the currently applied procedure, bringing along the indisputable advantage of limiting the occupancy time of the CT bunker.

5. Conclusions

This study presents an alternative method for refining the position of the ETS device, ensuring that the patient maintains a predefined position during treatment, which is crucial for the success of the therapy.

The innovative approach proposed in this study involves comparing and replacing the initial alignment of the ETS device, typically performed in the CT bunker, with an equivalent procedure executed in a dedicated room. This new procedure is supported by an OTS, which offers greater flexibility and optimization capabilities compared to the traditional method.

One of the significant advantages of this method is the potential reduction in the time spent on preparatory clinical activities.

The study was conducted concurrently with the standard method currently employed in the clinical workflow of CNAO. This parallel approach allowed for a direct comparison between the traditional method and the proposed alternative. The residuals between the ETS scan positions achieved with the two methods indicate that the new procedure can accurately align the ETS position. Furthermore, the ability to perform the procedure in a non-clinical environment adds another layer of flexibility to the treatment process. In conclusion, this study demonstrates the potential of the proposed method to enhance the efficiency and flexibility of setup optimization in ocular proton therapy.
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Data Availability Statement: The data presented in this study are available on request from the corresponding author. The data are not publicly available due to privacy.

Conflicts of Interest: The authors declare no conflicts of interest.

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