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# End-to-end quality assurance for stereotactic radiotherapy with Fricke-Xylenol orange-Gelatin gel dosimeter and dual-wavelength cone-beam optical CT readout

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**Title:****End-to-end quality assurance for stereotactic radiotherapy with Fricke-Xylenol orange-Gelatin gel dosimeter and dual-wavelength cone-beam optical CT readout****Author names and affiliations:**

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**Abstract**

*Purpose:* The end-to-end (E2E) quality assurance (QA) test is a unique tool for validating the treatment chain undergone by patients in external radiotherapy. It should be conducted in three dimensions (3D) to get accurate results. This study aims to implement these tests with Fricke-Xylenol orange-Gelatin (FXG) gel dosimeter and a newly developed dual-wavelength reading method on the Vista16™ optical Computed Tomography (CT) scanner (ModusQA) for three treatment techniques in stereotactic radiotherapy, on Novalis (Varian) and CyberKnife (Accuray) linear accelerators.

*Methods:* The tests were performed in head phantoms. Gel measurements were compared with planned dose distributions and measured by film and ion chamber measurements by plotting isodose curves and dose profiles, and by conducting a 3D local gamma-index analysis (2%/2mm criteria).

*Results:* Gamma passing rates were higher than 95 %. Point dose differences between treatment planning and gel and ion chamber measurements at the isocenter were less than 2.3 % for both treatments delivered on the Novalis accelerator, while this difference was higher than 4 % for the treatment delivered on the CyberKnife, highlighting a small overdosing of the tumor volume. A good agreement was observed between gel and film dose profiles.

*Conclusions:* This study presents the successful implementation of 3D E2E QA tests for stereotactic radiotherapy with FXG gel dosimetry and a dual-wavelength reading method on an optical CT scanner. This dosimetric method provides 3D absolute dose distributions in the 0.25 – 10 Gy dose range with a high spatial resolution and a dose uncertainty of around 2 % ( $k = 1$ ).

**Keywords:** 3D dosimetry, Fricke-based gel dosimetry, optical CT scanner, stereotactic radiotherapy.

## 1. Introduction

Stereotactic radiotherapy is a treatment technique that has become widespread in clinics for the last two decades. It enables the delivery of high doses with small irradiation fields (usually  $\leq 2 \times 2 \text{ cm}^2$ ) to treat tumor volumes that cannot be treated with conventional techniques while sparing the surrounding healthy tissues. This technique results in higher doses per fraction delivered to the target volumes. As it may be combined with dynamic techniques such as volumetric-modulated arc therapy (VMAT), automatic processes can be involved (inverse treatment planning, multileaf collimator (MLC), or gantry speed variation). They tend to increase the risk of missing the target volumes [1], leading to possible under-dosing or overdosing of the tumor volume and surrounding tissues. Therefore, these techniques require even more regular and adapted quality assurance (QA) tests. Among the available QA tests, end-to-end (E2E) ones allow for verifying and validating the whole treatment chain undergone by patients in clinics, from imaging to treatment delivery using anthropomorphic phantoms [1,2]; they must be able to detect any dose or spatial errors.

Consequently, these QA tests should be performed ideally by measuring three-dimensional (3D) dose distributions with a high spatial resolution. However, the dosimeters currently used in clinical routine (ion chambers, radiochromic films, etc.) are poorly suited as they only measure point or 2D dose distributions. Even if 3D arrays of detectors are available, they require interpolation calculations to provide 3D dose distributions with a low spatial resolution [3].

Therefore, gel dosimeters are promising candidates for implementing this QA test as they can measure 3D dose distributions with a high spatial resolution. In the last decade, several papers have reported on the implementation of 3D E2E QA tests with dosimetric gels [4–7], which are mainly Fricke-based gels, polymer gels and PRESAGE™ [8,9], and their associated readout technique such as Magnetic Resonance Imaging, optical Computed Tomography (CT) and X-ray CT.

In a previous study, Rousseau *et al* 2022 [10] developed a new dosimetric method to provide accurate 3D dose measurements, with a high spatial resolution and a linear dose-response, on a dose range representative of stereotactic and dynamic radiotherapy treatments, *e.g.* 0.25 – 10 Gy. It was based on Fricke-Xylenol orange-Gelatin (FXG) gel and a novel dual-wavelength reading method implemented on the cone-beam Vista16™ optical CT scanner (ModusQA, London, Ontario, Canada). This reading method enabled scanning of low and high doses in a single dosimeter by combining the dose distributions measured at two wavelengths (using two distinct light sources): one at 590 nm for the low doses and one at 633 nm for the high doses. In comparison, only doses below 4 Gy could be read with a single scan at 590 nm for FXG gel dosimeters [11,12]. This global dosimetric method was characterized and validated for absolute dose profile measurements in small-field dosimetry.

The present study aims at implementing this dosimetric method to perform 3D E2E QA tests on the Novalis TrueBeam STx (Varian) and CyberKnife M6 (Accuray) accelerators in anthropomorphic head phantoms. Additional measurements with the Razor Nano Chamber (IBA) and EBT3 Gafchromic films (Ashland) are also performed at the isocenters and in slices passing through the isocenters of the treatment plans delivered on the Novalis accelerator to compare them to the gel measurements. The main objectives are to evaluate the performances obtained with this dosimetric method and its suitability to validate the treatments delivered in this study to consider the opportunity of its future implementation in radiotherapy centers.

## 2. Materials and methods

### 2.1. FXG gel preparation

The FXG gel composition selected for this study was described in Rousseau *et al* 2022 [10] and exhibited a high-sensitive linear dose-response up to 10 Gy. The FXG gel dosimeters were prepared with ultrapure deionized water, 5 % wt gelatin from porcine skin (strength 300, Type A), sulfuric acid to reach a pH of 1.6, 0.3 mM ferrous ammonium sulfate and 0.09 mM xylanol orange. They were poured into Teflon-FEP (Fluorinated Ethylene Propylene) cylindrical flasks of 3.9 cm diameter and 6.3 cm height with ETFE (Ethylene Tetrafluoroethylene) caps. The gel dosimeters were prepared one day before their irradiation and placed in the irradiation room at least eight hours before irradiation for thermal stabilization. They were read up to 1 hour after irradiation (see Section 2.5 for more details).

### 2.2. Implementation of 3D end-to-end quality assurance tests

3D E2E QA tests were implemented in two French radiotherapy centers on linear accelerators dedicated to stereotactic radiotherapy: the Novalis TrueBeam STx (Varian Medical Systems, Palo Alto, CA, US) at Institut de Cancérologie de l'Ouest (ICO) in Angers and the CyberKnife M6 (Accuray, Sunnyvale, CA, US) at Gustave Roussy (GR) in Villejuif.

The STEEV phantom (CIRS, Inc. Norfolk, VA, US) and the CyberKnife head-and-neck phantom (Accuray) were used on the Novalis and the CyberKnife accelerators, respectively (Fig. 1 (a) and (b)). These phantoms were selected as they are already available and used in the clinics, thus facilitating a future implementation of 3D E2E tests with gel dosimetry without the need to create a new phantom. A water-equivalent plastic insert was designed to fit a FXG gel flask in the cavity of each phantom (Plastic Water, CIRS). The outer dimensions of the two inserts were 9.4 x 6.4 x 6.4 cm<sup>3</sup> and 9.1 x 6.3 x 6.3 cm<sup>3</sup> for the STEEV and CyberKnife phantoms, respectively (Fig. 1 (c)). The orientation of the phantoms with their left/right, feet/head and back/front directions are represented in Fig. 1 (d) for clarity.

In this study, we (researchers and medical physicists) conducted the E2E tests, for each phantom and linear accelerator, following these steps [2]:

- Acquisition of CT images of the head phantom containing a FXG gel flask (the gel flask not being re-used later),
- Creation of treatment plans on the CT images with a TPS (Treatment Planning System),
- Optical measurements with the Vista16™ scanner and determination of FXG gel calibration curves at 590 nm and 633 nm in water,
- Repositioning of the head phantom containing a gel flask with the on-board imaging system of the treatment unit before irradiation (ExacTrac system (Brainlab, Heimstetten, Germany) on the Novalis accelerator and kVCT image-guided system on the CyberKnife accelerator),
- Delivery of each treatment in two gel flasks,
- Optical reading of the gel flasks, analysis of the results and comparison with the dose distributions planned by the TPS.

The next sections describe in detail these steps.

### 2.3. FXG gel dose calibration

Identical gel flasks were used for calibration and QA measurements to avoid volume effects and thus perform absolute dosimetry. The FXG gel was calibrated in terms of absorbed dose to water with the multi-flask calibration procedure. For each linear accelerator, twelve FXG gel flasks were irradiated at known doses on the 0.25 – 4 Gy and 2 – 10 Gy dose ranges for the reading of low doses at 590 nm and high doses at 633 nm, respectively (see Section 2.5). Each gel flask was irradiated within a water tank

following the TRS 398 reference conditions (source-to-axis distance of 100 cm, field size of 10 x 10 cm<sup>2</sup> and reference depth of 10 cm).

This calibration was performed on the Novalis accelerator with a 6 MV FFF (Flattening Filter Free) photon beam and a 1400 MU/min dose rate. For the E2E test implemented on the CyberKnife, the calibration could not be performed under the TRS 398 reference conditions due to the distinctive features of this accelerator (reference circular field of 6 cm diameter and 80 cm reference source-to-axis distance) [13]. Therefore, it was performed on another accelerator, a TrueBeam (Varian), with a 6 MV FFF photon beam and a 1000 MU/min dose rate.

Each gel flask was read with the Vista16™ scanner at 590 nm or 633 nm, depending on the dose level, to measure a 3D optical attenuation map (see Section 2.5 for more details about the optical CT readout). An optical attenuation value  $\Delta\mu$  (in cm<sup>-1</sup>) was averaged in a cubic ROI (Region Of Interest) of 1 cm<sup>3</sup> selected at the center of each flask irradiated at a known dose. Linear calibration curves  $D = a_\lambda \times \Delta\mu + b_\lambda$  ( $\lambda = 590$  nm or 633 nm) were then determined by applying a linear regression on the spanned dose ranges at each wavelength [10].

The same batch of gel was used for calibration and E2E QA purposes so that the inter-batch reproducibility was not taken into account in the uncertainty budget [10]. Irradiations were all performed within one day to obtain the same thermal and spontaneous oxidation histories in the gel flasks.

As Fricke-based gels are water-equivalent dosimeters [14], the measured dose distributions with FXG gel could directly be compared with the dose distributions calculated by the TPS, whether these distributions were given in terms of absorbed dose to water or in terms of absorbed dose to medium.

## 2.4. Treatment planning

The stereotactic plans used for the implementation of E2E QA tests with FXG gel dosimetry were created by the medical physicists on the CT images of the STEEV and the CyberKnife head phantoms that contained a gel flask. All CT images were acquired with a Somatom CT scanner (Siemens Healthineers) available in each radiotherapy center. A thermoplastic mask covered the STEEV phantom for immobilization during imaging and treatment; the CyberKnife head phantom was used without any mask.

Three plans (two for the STEEV phantom and one for the CyberKnife phantom), using three different treatment techniques of stereotactic radiotherapy, were created to place precisely volumes of interest (Planning Target Volume (PTV) and Organs At Risk (OARs)) inside the gel flask on the CT images.

For the Novalis accelerator, a first treatment was planned with conformal arcs using the TPS iPlan (Brainlab) with its XVMC (X-ray Voxel-based Monte Carlo simulation) algorithm to compute absorbed doses to medium. The planned dose distribution displayed a calculation grid spacing of 0.98 x 0.98 x 1 mm<sup>3</sup>. A spherical brain tumor of 1.5 cm diameter was delineated. The minimum and maximum doses delivered in the PTV were 5.1 Gy and 7.2 Gy, respectively (Fig. 2 (a)). Four non-coplanar arcs of 6 MV FFF beams with a 1400 MU/min dose rate were defined, with rotations of the treatment table at 70°, 30°, 330° and 290°. This plan was relatively simple and similar to those used for the E2E QA tests performed annually at the ICO.

A more complex dose map was also created for the Novalis accelerator with a 360° two-arc VMAT plan and a calculation grid spacing of 1.25 x 1.25 x 1 mm<sup>3</sup> using the TPS Eclipse (Varian) with Acuros XB algorithm. A heterogeneous dose distribution, computed in terms of absorbed dose to medium, was prescribed to a brain tumor of complex shape with three dose levels (4.9 Gy, 5.5 Gy and 6.5 Gy) to apply a steep gradient in the PTV. The maximum dose delivered was 6.9 Gy (Fig. 2 (b)).

6 MV FFF beams with a 1400 MU/min dose rate were used. A fictional OAR of convex shape was also added near the PTV to increase the complexity of the planned dose distribution.

For the CyberKnife accelerator, the TPS Precision (Accuray) and RayTracing algorithm were used to generate a plan that computed absorbed doses to water. The voxels of the dose distribution were of dimensions  $0.7 \times 0.7 \times 1 \text{ mm}^3$ . The plan consisted of 6 MV FFF beams delivered to a brain tumor of volume similar to a sphere, with a 1000 MU/min dose rate and a 20 mm fixed collimator opening. A dose of 7 Gy was prescribed at the 80 % isodose line, and the maximum delivered dose was 8.8 Gy (Fig. 2 (c)).

## 2.5. Dual-wavelength optical CT readout

The FXG gel flasks used for calibration and QA measurements were read with the Vista16™ scanner. A pre-irradiation reference scan and a post-irradiation data scan of each dosimeter were acquired at one (for calibration purpose) or two (for QA measurements) reading wavelengths, 590 nm and 633 nm, with 2000 projections for each scan that lasts approximately 5 min. The post-irradiation scanning time constraints were previously determined in Rousseau *et al* 2022 [10] for FXG gel dosimetry associated to the Vista16™ scanner readout. It was stated that the data scans must be performed at least 20 min after irradiation to reach chemical reaction completion, and within 60 min to induce a spatial deformation of the dose distribution, due to diffusion effects in the gel matrix, unnoticeable when the measured dose distribution displays a voxel size of  $0.5 \times 0.5 \times 0.5 \text{ mm}^3$ .

Two different algorithms were applied for CT reconstruction. As it has been commonly used for cone-beam optical CT reconstruction with gel dosimetry, the Feldkamp–Davis–Kress (FDK) algorithm [15], based on filtered backprojection, was used in this study with a Hamming filter. The iterative OSC-TV (Ordered Subsets Convex with regularization via Total Variation) algorithm is a more recent algorithm and was also used as it tends to reduce noise and artifacts in the reconstructed distributions [16,17]. All reconstructions were performed with voxels of dimensions  $0.5 \times 0.5 \times 0.5 \text{ mm}^3$ . The matching liquid in the tank of the scanner was a mixture of 10 % wt propylene glycol – deionized water [18].

Calibration curves determined at 590 nm and 633 nm were applied on the measured optical attenuation maps to obtain dose maps for each QA flask. The dual-wavelength reading method developed in Rousseau *et al* 2022 [10] was then used. For this purpose, the low doses were selected in the dose distribution measured at 590 nm, while the high doses were selected at 633 nm, thus avoiding saturation in optical attenuation that was present at 590 nm for doses higher than 4 Gy. In this study, the threshold dose between the two distributions was adopted at 2.5 Gy.

The post-irradiation scanning times for each wavelength and the labels of the gel flasks are reported in Table 1. The time constraint of 60 min was met for all configurations except for readings at 633 nm of F1 and 590 nm of F2, as the conformal treatment delivered in these flasks lasted 20 minutes compared to the shorter delivery time for the other two treatments (10 minutes).

## 2.6. Dose distribution analysis

For all gel flasks, a mark was made at their top to enable a reproducible repositioning between reference and data scans. This mark was always placed at the same position in the head phantoms for the E2E QA measurements so that we could determine a fixed rotation angle to apply to the measured 3D dose distributions to obtain the same orientation as the TPS ones. Translations were then applied to the measured dose distributions in the three spatial dimensions so that the flask walls in the measured dose maps would align with those on the CT images.

Measured and planned dose distributions were analyzed with in-house programs developed using Python software with Matplotlib, NumPy, SciPy, PyMedPhys and Pydicom libraries. Cylindrical ROIs of 34 mm diameter and 53.5 mm height, corresponding to the volumes of gel inside the flasks,

were selected in the dose maps. The comparison between measured and TPS dose distributions was performed by displaying isodose curves and dose profiles.

We also conducted a 3D gamma-index analysis [19]. The dosimetric and spatial uncertainties of our FXG gel measurements were estimated and adequate gamma passing (GP) criteria were thus selected. The overall dosimetric uncertainty was evaluated in a previous study and was about 2 % for the coverage factor  $k = 1$  [10]. For the overall spatial uncertainty, the following sources were considered. Gel flasks were repositioned between their pre- and post-irradiation scan with an associated error of  $1^\circ$  on the rotation angle, leading to a spatial uncertainty of 0.3 mm (considering the radius  $R = 17$  mm of the ROI) along the  $x$  or  $y$ -axis. For the translational registration of the measured dose maps, a spatial uncertainty of 0.5 mm (voxel size) was considered in the three directions. This uncertainty was also associated with repositioning of the head phantom with the on-board image-guided system. An error of  $1^\circ$  on the positioning of the gel flask in the head phantom was accounted for and induced a 0.3 mm spatial uncertainty. As reported in Table 2, the overall spatial uncertainty was about 2 mm. Therefore, we conducted a 3D local gamma-index analysis with 2%/2mm GP criteria and a 10 % dose cutoff.

## **2.7. Point and 2D dose measurements**

Additional point and planar absolute dose measurements were conducted for both conformal and VMAT treatments delivered on the Novalis accelerator with the Razor Nano Chamber (IBA Dosimetry GmbH, Schwarzenbruck, Germany) and EBT3 Gafchromic films (Ashland Global Specialty Chemicals Inc., Wilmington, Delaware, US) to compare them to our gel-based measurements. However, no additional absolute dose measurements were performed for the CyberKnife treatment, as the CyberKnife head phantom is not designed to conduct ion chamber measurements (or any other dosimeter presenting a cable) and because film dosimeters are not currently used to perform dosimetric E2E QA tests at Gustave Roussy on the CyberKnife.

### *2.7.1. Film measurements*

2D E2E QA tests were performed with EBT3 films. The same batch of films was used for the calibration and QA tests. A 12-points calibration curve ranging from 0.5 Gy to 7 Gy was determined under reference conditions in water-equivalent slabs. The films were read on an Epson 10000XL scanner with a square pixel size of 0.26 mm. The calibration curve in terms of absorbed dose to water was determined following the multichannel method of Micke *et al* 2011 [20].

For both E2E QA tests, squared films of 4 cm side were prepared and placed in the STEEV phantom with their dedicated insert and positioned at the isocenter of the plans. Two film orientations were selected: one in the front/back direction (axial slice) and the other in the head/feet direction (coronal slice), for a total of eight films (two films per orientation). These films were scanned in the same conditions as the calibration films. Optical density distributions measured by film were converted into dose distributions using the calibration curve and an ImageJ plugin. The uncertainty on the absorbed dose measured with this dosimetric method was estimated to be at least 3 % at  $k = 1$  [21]. The analysis of these measured dose distributions was conducted with Python.

To simplify the analysis, we checked if the dose distributions planned on the CT images containing either a gel flask or a film, with their respective insert, were similar enough to be considered equivalent. Therefore, we conducted a 3D global gamma-index analysis between these two planned dose distributions with 1%/1mm GP criteria and without any dose cutoff. Very high GP rates of 99.8 % and 99.4 % were found for the conformal and VMAT plans, respectively, thus allowing us to directly compare the dose distribution planned on the CT images with the gel flask to the gel and film-based measurements.

The dose distributions planned by TPS and measured by film and gel were finally compared by plotting the dose profiles passing through the isocenter of these distributions and by conducting a 2D local gamma-index analysis with 2%/2mm GP criteria and a 10 % dose cutoff.

#### *2.7.2. Ion chamber measurements*

Point measurements were performed with the Razor Nano Chamber at the isocenter of the plans in the STEEV phantom. A cross-calibration had been previously conducted in water against an ion chamber traceable to a primary standard. This ion chamber presented a small sensitive volume corresponding to a sphere of 1 mm radius. Even if only 1D information were given with this dosimeter, lower uncertainties (compared to film-based measurements) of about 2 % at  $k = 1$  were associated with these measurements. Three measurements were undertaken and averaged for each plan.



### 3. Results

#### 3.1. Conformal plan

Two gel flasks, F1 and F2, were used to perform the E2E QA test of the conformal plan on the Novalis accelerator. For clarity, the following figures (except for the dose profiles) display the results of only one flask and one algorithm (arbitrarily F2 and the FDK algorithm), as the results were similar for both flasks and both algorithms. Nevertheless, all results are discussed here.

A very good agreement between measured and TPS isodose curves (80 %, 60 %, 40 % and 20 %) was observed in Fig. 3 (a). Excellent GP rates, all higher than 99.0 % for both flasks and algorithms (FDK and OSC-TV), are also reported in Table 3 for a 3D local analysis with 2%/2mm GP criteria and 10 % dose cutoff. The failing points were located at the edges of the flask in the gamma maps (see sagittal slice in Fig. 4 (a)). Besides, when looking at the measured and TPS dose profiles (Fig. 5 (a)), minor deviations were observed at the edges of the profiles, with measured dose values being lower than TPS ones. These deviations were slightly higher for F1 than F2 due to the scanning time of F1 at 633 nm (for the measurement of high doses) that exceeded the 60 min maximum time recommended to neglect diffusion effects in the gel matrix (Section 2.5).

#### 3.2. VMAT plan

The VMAT plan was delivered with the Novalis accelerator in the flasks F3 and F4. As in Section 3.1, measured dose distributions were similar between both flasks and both algorithms, so the subsequent figures only display the results of F3 with FDK reconstruction.

An excellent agreement was found between 90 %, 80 %, and 60 % measured and computed isodose curves (Fig. 3 (b)), while a slight difference of about 2 mm between 40 % isodose curves was observed. The local 3D gamma-index analysis displayed GP rates higher than 96.7 % for each flask and algorithm (Table 3). The failing points were observed, in the gamma maps of Fig. 4 (b), in the OAR volume (middle left of the flask in the axial and coronal slices), and in regions of doses lower than 3.5 Gy (at the top in the axial slice, and the top left and bottom right in the sagittal slice). An excellent agreement was found between measured and TPS dose profiles, except in the OAR volume, where the measured doses were higher than the planned ones (see dose values where position  $\leq -10$  cm in Fig. 5 (b) in the right/left direction).

#### 3.3. CyberKnife plan

The treatment for the CyberKnife was delivered in flasks F5 and F6. As in Sections 3.1 and 3.2, the figures display the results for only one flask, F5, and for the FDK algorithm. Measured and TPS 90 %, 80 %, 60 % and 40 % isodose curves were in excellent agreement (Fig. 3 (c)). GP rates for the 3D local analysis were higher than 98.8 %, whatever the algorithm and flask considered (Table 3). The failing points in the gamma maps of Fig. 4 (c) were all in the PTV. Comparing the measured and TPS dose profiles, measured doses in the high doses region were, indeed, higher than the planned ones. However, this discrepancy was not observed for the lower doses, for instance, in the measured profiles along the back/front direction that displayed an excellent agreement with the planned profile for doses below 6 Gy (Fig. 5 (c)). A dose deviation of 4.0 % was calculated between TPS and gel measurements at the center of the PTV (Table 5).

#### 3.4. Film and ion chamber measurements for conformal and VMAT plans

The dose profiles selected at the center of the planned and measured by film dose distributions for the conformal and VMAT treatments delivered on the Novalis accelerator are displayed in Fig. 6. The measured dose profiles in the axial slice of the conformal plan and the coronal slice of the VMAT plan were in good agreement with the planned ones. However, discrepancies in the high doses regions were

observed between both profiles measured by film for the coronal slice of the conformal plan and for the axial slice of the VMAT plan. Consequently, the measurements performed with film dosimetry appeared less reproducible than with FXG gel dosimetry in our study (see Fig. 5 (a) and (b)).

Both dose profiles measured by film and FXG gel dosimetry were then averaged for each configuration (vertical/horizontal direction, coronal/axial slice and conformal/VMAT plan) and are reported, with planned dose profiles, in Fig. 7. All the dose profiles were similar for the conformal treatment, with only a slightly better agreement at the edges of the profiles between film and gel measurements. This discrepancy with the planned dose distribution is also visible in the 2D gamma maps of Fig. 8 (for a 2D local gamma-index analysis with 2%/2mm GP criteria and 10 % dose cutoff), as high gamma values, around 0.5 – 0.8, were found in this area between film and gel measurements compared to the TPS distribution. The results displayed in this figure correspond to the best ones obtained among each film and gel flask for one configuration. However, despite this slight discrepancy, GP rates were higher than 95.8 % for each dosimeter and slice (average values for two films and two gel flasks, see Table 4).

Looking at the planned and measured (by film and gel) dose profiles for the VMAT plan in Fig. 7, an excellent agreement was found between all the profiles, except for the OAR region (position  $\leq -10$  cm in the horizontal profiles), where doses measured by gel were higher than the planned ones and the ones measured by film. This discrepancy can also be observed in Fig. 8 (b), where failing points of the 2D gamma-index analysis were located in the OAR region when comparing gel measurements with the TPS distribution. Yet, all GP rates were still higher than 96.1 % for each dosimeter and slice.

TPS and average measured dose values (for two and three measurements for gel and ion chamber detectors, respectively) at the isocenter of the conformal and VMAT plans are reported in Table 5. For the conformal plan, dose differences below 0.3 % were obtained between TPS data and both measurements. Larger dose differences, of 1.6 % and 2.3 % for the VMAT plan, were obtained between TPS data and ion chamber and gel measurements, respectively. However, planned and measured dose values agreed within experimental uncertainties in these two cases. Besides, gel and ion chamber measurements displayed similar dose values for both plans.

## 4. Discussion

This study presented the implementation of 3D E2E QA tests with a new dosimetric method based on FXG gel and a dual-wavelength readout on the Vista16™ optical CT scanner. The tests were conducted for intracranial tumors in the STEEV and CyberKnife head phantoms for three different techniques of stereotactic radiotherapy: conformal and VMAT techniques on the TrueBeam Novalis STx accelerator (Varian) and a stereotactic plan on the CyberKnife (Accuray).

2D and 3D local gamma-index analyses between planned and measured dose distributions (by film and gel dosimeters) with 2%/2mm GP criteria and 10 % dose cutoff displayed GP rates higher than 95 % for the conformal and VMAT plans on the Novalis accelerator. Point measurements at the isocenters of these plans also revealed a maximum of 2.3 % dose difference between planned and measured doses (by ion chamber and gel detectors). Based on Miften *et al* 2018 [22], we selected the following criteria for evaluating the E2E QA analysis: a GP rate higher than 95 % and a difference between planned and measured doses lower than 3 % for a point measurement in a high doses region. Therefore, the E2E QA tests implemented on this accelerator were validated for both treatments.

However, for the VMAT plan, the doses measured by gel in the low doses region of the OAR volume were higher than the planned ones (Section 3.2). As doses below 0.5 Gy were accurately measured in Section 3.1, we deduced that this discrepancy was not due to diffusion effects in the gel matrix. Therefore, two other reasons could be considered. The first would be that the treatment was not delivered as expected, as significant dose constraints were applied (maximum dose < 4.5 Gy and mean dose < 1 Gy in the OAR volume) that may have been difficult to fulfill. Nevertheless, measured by film dose distributions agreed with the TPS dose distribution in the OAR region. Therefore, this discrepancy most probably comes from the physical models of the optical CT reconstruction algorithms that may contain approximations that have induced measurement errors in convex regions, such as the OAR volume. Future investigations should be undertaken to adapt the algorithms' physical models to solve this issue.

For the treatment delivered on the CyberKnife, the GP rates were higher than 98.8 % for the 3D local analysis between planned and gel measurements. However, the measured dose in the high doses region displayed a deviation of 4.0 % compared to the planned one. As doses were accurately measured by gel in the PTVs for the treatments delivered on the Novalis accelerator (see dose profiles in Fig. 5 (a) and (b)), this deviation was most probably due to the delivery of the treatment. Therefore, if we consider our previous criteria for evaluating this E2E QA test, the test we implemented on the CyberKnife did not pass.

In overall, the dosimetric method used in this study, based on FXG gel and a dual-wavelength readout, was able to measure simultaneously low doses in healthy tissues surrounding the tumor volume (< 0.5 Gy) and high doses in the tumor volume (up to 10 Gy). As far as we know, this dose range had never been used before for 3D measurements with FXG gel dosimetry, going up to 4 Gy only [11,12,23]. Moreover, this dosimetric method could be easily implemented in clinics as the gel flasks can be inserted in commercial anthropomorphic phantoms. This method is also the first one to measure accurate absolute 3D dose distributions using the multi-flask calibration procedure. At last, the uncertainty on the absorbed dose with this dosimetric method was about 2 % at  $k = 1$  [10].

However, in the near future, the dual-wavelength reading method used in this study should be optimized to become less time-consuming by replacing the two light sources currently used (emitting at 590 nm and 633 nm) into one light source able to switch its wavelength of emission easily. Automatic registration should also be implemented in the future, as the one used in this study was manual and therefore time-consuming.

Nonetheless, given the excellent results obtained with this dosimetric method (absolute 3D dosimetry performed on the 0.25 – 10 Gy dose range and 3D local gamma-index analysis with

2%/2mm GP criteria resulting in GP rates higher than 95 %), the implementation of 3D E2E QA tests in radiotherapy centers with this method is promising.

## 5. Conclusion

FXG gel dosimetry and a dual-wavelength reading method on the Vista16™ optical CT scanner were used to implement 3D E2E QA tests for three different stereotactic radiotherapy applications on the Novalis TrueBeam STx and CyberKnife linear accelerators. 3D local gamma-index analyses of 2%/2mm passing criteria and 10 % dose cutoff were conducted between gel measurements and radiation treatment planning, resulting in gamma passing rates higher than 95 % for each application. Point dose differences between gel measurements and treatment planning in the high doses region of each plan were lower than 2.3 % for both QA tests performed on the Novalis, while they were of 4 % for the QA test on the CyberKnife. Therefore, we concluded that only E2E QA tests conducted on the Novalis accelerator were validated. Point and 2D dose measurements by ion chamber and radiochromic films agreed with the results obtained with gel dosimetry.

Based on these results, the dosimetric method used in this study provided excellent dosimetric performances with 3D absolute dose measurements associated with an uncertainty of 2 % ( $k = 1$ ). However, the dual-wavelength reading method used on the CT scanner still necessitates an optimization to be less time-consuming when used, and the reading artifact observed in the convex OAR region of one of the QA tests must be investigated further by studying the physical models of the algorithms used for the CT reconstruction of gel measurements.

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## Figure captions:

Fig.1: (a) STEEV head phantom (CIRS), (b) CyberKnife head-and-neck phantom (Accuray), (c) water-equivalent plastic insert designed for 3D dosimetry with FXG gel for the STEEV phantom and (d) orientation of each head phantom (feet/head, front/back and left/right directions).

Fig. 2: Axial views of the dose distributions computed by TPSs (top) and of the volumes of interest (PTV in purple and OAR in blue) inside the gel flask (bottom) for (a) conformal and (b) VMAT treatments on the STEEV phantom for the Novalis accelerator at ICO, and (c) the treatment on the CyberKnife head-and-neck phantom for the CyberKnife accelerator at GR.

Fig. 3: (a) 80 %, 60 %, 40 % and 20 % isodose curves of the measured and TPS dose maps at the isocenter of the conformal plan. (b)-(c) 90 %, 80 %, 60 % and 40 % isodose curves of the measured and TPS dose maps at the isocenter of the VMAT and CyberKnife plans, respectively. From left to right: axial, sagittal and coronal slices. In black: calculated isodose curves; in gray: measured isodose curves. In background: measured dose distributions (F2, F3 and F5 with FDK reconstruction).

Fig. 4: Gamma maps (3D local analysis, 2%/2mm GP criteria and 10 % dose cutoff) between gel measurement (FDK reconstruction) and TPS dose at the isocenter of the (a) conformal, (b) VMAT and (c) CyberKnife plans. From left to right: axial, sagittal and coronal slices.

Fig. 5: Measured and TPS dose profiles at the isocenter of the (a) conformal, (b) VMAT and (c) CyberKnife plans. From top to bottom: profiles along the right/left, back/front and feet/head directions.

Fig. 6: (a) Vertical and (b) horizontal dose profiles selected at the center of the TPS and measured by film dose distributions for the conformal and VMAT plans in the axial and coronal slices.

Fig. 7: (a) Vertical and (b) horizontal dose profiles selected at the center of the TPS and measured by gel and film dose distributions for the conformal and VMAT plans in the axial and coronal slices.

Fig. 8: 2D gamma maps (local analysis, 2%/2mm GP criteria and 10 % dose cutoff) between (a) TPS and measured by film dose distributions and (b) TPS and measured by gel dose distributions for the conformal and VMAT plans.

Table 1: Labels of the gel flasks for each treatment and post-irradiation scanning times at each wavelength.

Treatment technique	Flask label	Post-irradiation scanning time (min)	
		590 nm	633 nm
Conformal	F1	24	78
	F2	73	20
VMAT	F3	23	52
	F4	56	20
CyberKnife	F5	45	20
	F6	56	21



Table 2: Spatial uncertainties associated to the E2E QA measurements performed with FXG gel dosimetry ( $k = 1$ ).

Sources of spatial uncertainty	Expression and numerical value
Flask repositioning during readings	$\delta y = R \times \sin(\theta)$ ( $\theta = 1^\circ$ and $R = 17$ mm)
Registration of the measured dose maps with respect to CT images	$\Delta x = 0.5$ mm; $\Delta y = 0.5$ mm; $\Delta z = 0.5$ mm
Image-guided repositioning of the head phantom	$\Delta X = 0.5$ mm; $\Delta Y = 0.5$ mm; $\Delta Z = 0.5$ mm
Flask positioning in the head phantom	$\delta Y = R \times \sin(\alpha)$ ( $\alpha = 1^\circ$ and $R = 17$ mm)
<b>Overall spatial uncertainty</b>	$\sqrt{(\Delta x + \Delta X)^2 + (\Delta y + \delta y + \Delta Y + \delta Y)^2 + (\Delta z + \Delta Z)^2} =$ <b>2.1 mm</b>

Table 3: GP rates (3D local analysis, 2%/2mm GP criteria and 10 % dose cutoff) for each gel flask used for the E2E tests and for FDK and OSC-TV algorithms compared to the planned dose distributions.

<b>Gamma-index (%)</b>	<b>FDK</b>	<b>OSC-TV</b>
<b>F1</b>	99.4	99.0
<b>F2</b>	99.2	99.5
<b>F3</b>	98.6	98.2
<b>F4</b>	96.7	98.4
<b>F5</b>	99.1	99.7
<b>F6</b>	98.8	98.9

Table 4: Average GP rates (2D local analysis, 2%/2mm GP criteria and 10 % dose cutoff) for two films and two gel flasks compared to the conformal and VMAT planned dose distributions.

<b>Gamma-index (%)</b>	<b>Slice</b>	<b>Film</b>	<b>Gel</b>
<b>Conformal</b>	Coronal	95.8	99.9
	Axial	100	99.9
<b>VMAT</b>	Coronal	99.4	96.1
	Axial	99.4	97.8

Table 5: TPS and average measured dose values at the isocenter of the plans, and differences between measured and planned doses (number in parentheses).

Isocenter	Planned dose (Gy)	Measured dose (Gy)	
		Ion chamber	Gel
Conformal	7.08	7.06 ± 0.13 (-0.3 %)	7.07 ± 0.16 (-0.1 %)
VMAT	6.60	6.71 ± 0.14 (1.6 %)	6.75 ± 0.18 (2.3 %)
CyberKnife	8.47		8.81 ± 0.17 (4.0 %)

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