Personalized PseudoPatient™ for patient-specific plan verification in advanced radiotherapy applications

Clinical white paper

The wide use of stereotactic radiosurgery (SRS), intensity modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT) treatment approaches for the management of a variety of brain lesions, has resulted in safer treatments and a better quality of life for patients than ever before[1]. Contemporary single-isocenter linac-based SRS is an effective first-line treatment for patients with brain metastases, compared to whole brain radiotherapy[2,3]. At the same time, treatment planning and dose delivery are becoming ever more customizable to individual patients[4]. Plans characterized by high levels of conformity and steep dose gradients from the periphery of the target to surrounding tissue are created, using a single isocenter and non-coplanar arcs[5]. Such complex treatments and the consequences of errors when delivering high-dose fractions of radiation just millimeters beyond their intended site, can have a far-reaching physiological impact[6]. Therefore, the need for pre-treatment dose verification in the actual patient's anatomy in order to minimize the possibility of unintended exposure, which can compromise tumor control probability (TCP) and normal tissue complication probability (NTCP) treatment objectives[7,8], is never more critical.

Patient-specific QA

Although current patient-specific quality assurance (QA) techniques for SRS/SRT, IMRT and VMAT are able to detect critical dose errors, the resulted "in-vivo" dose distributions are employed as "virtual measurements" of patient dose[4]. This is furtherly supported by the fact that some of the commercially available solutions do not allow measurements in the exact treatment position, in cases where non-coplanar arcs are involved, resulting in measured dose distributions different from the ones obtained in the actual patients' geometry[9]. Calculations and measurements are performed in standard shaped phantoms and dose is then reconstructed within the patient anatomy. Plan evaluation is based on IMRT QA performance metrics, such as gamma passing rates, of controversial predictive power for clinical dose errors[4]. More generally, IROC Houston measurements through time indicate inconsistencies in QA results, failure of detection of unacceptable plan delivery and highlight the need for the patient-specific QA process to be optimized[10]. This fact creates the necessity of a personalized solution which includes both dosimetry and imaging accuracy verification. Ultimately, QA tests must be performed by means that assess both the individual and integrated localization and dosimetric components in an End-to-End manner.

Lifelike human anatomy

The 510(k) FDA cleared personalized PseudoPatient™ (PPP) is created from actual patients' planning CT scans using 3D-printing technology and bone-mimicking material, while the phantom is filled with water that serves as the soft tissue equivalent. The level of dosimetric equivalency between the actual patient and the phantom in the high energy photon fields used herein is evaluated elsewhere[11]. It's advantage though, is the realistic bone and soft tissue contrast in both MR and CT imaging. This unique feature enables during image guidance the direct fusion of the phantom images with the real patient's, and therefore the implementation of literally end-to-end patient-specific pre-treatment plan verification in intracranial applications, since the exact same clinical workflow can be followed (Figure 1).

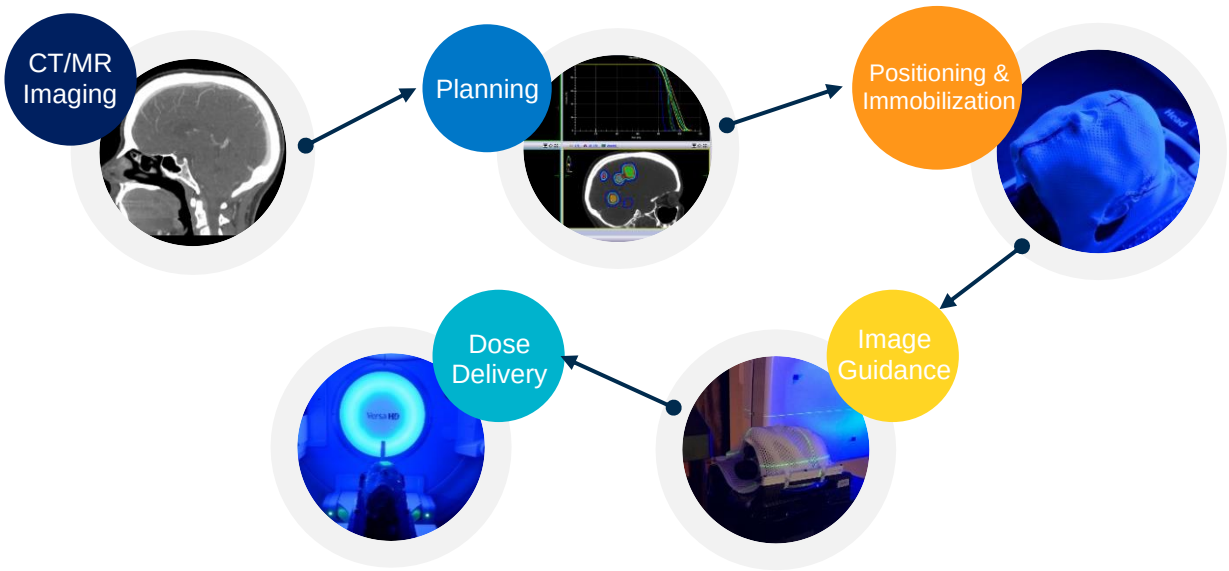

Figure 1. The workflow using Personalized PseudoPatient™. The entire treatment chain is implemented assuming that the subject under treatment is the real patient.

Patient-Centric E2E QA

PPP was developed to address one strategic need of a patient brain radiotherapy QA session: the implementation of direct measurements of the dose that is actually deposited within the patient planning target volume (PTV) and selected organs at risk (OARs). This is achieved by treating the phantom as if it is the real patient and delivering the exact same plan intended for the patient to the patient's exact anatomical replica. Dose verification is performed using ion chamber dosimetry that remains the gold standard for point dose measurements. Treatment planning system (TPS) calculated dose values can be directly compared with measurements. For the purpose of this study ten (10) patient VMAT plans, including either stereotactic or re-irradiation cases of primary or recurrent brain or head and neck tumors were selected and evaluated. Phantom design and construction was based on the anonymized planning CT DICOM images of each patient (Figure 2) using the methodology described in Makris et al[11]. Briefly, a 3D-printer was used to construct a hollow phantom that duplicates the patient anatomical geometry, in terms of external contour and cranial bone anatomy. Special inserts were also constructed in order to position either a semiflex PTW (active volume of 0.125 cc) or a CC01 IBA (active volume of 0.01 cc) ionization chamber within the PTV and/or OARs, according to the corresponding DICOM RT Structure set file of each patient (Figure 2a, c).

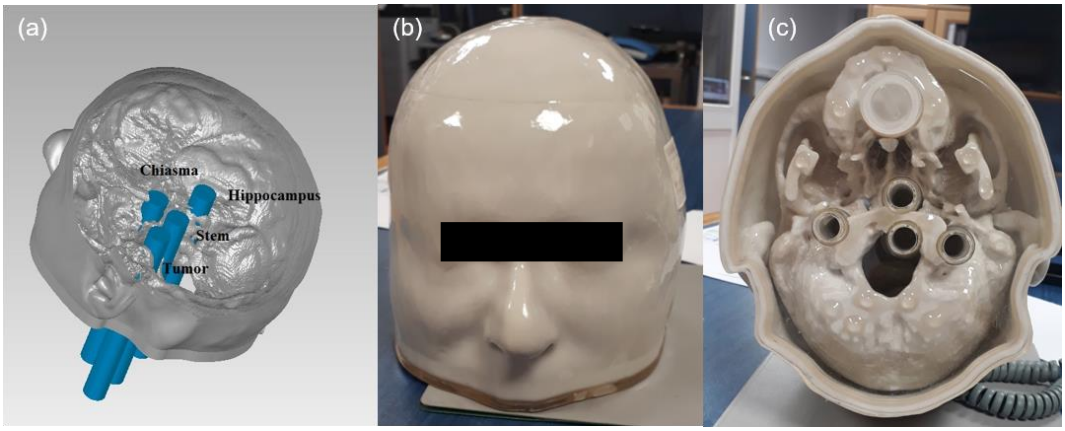

Figure 2. (a) The created 3D model that duplicates a specific patient's anatomy and the designed special inserts in order to position the sensitive volume of the department's specific type ionization chamber within the PTV and the OARs, according to the corresponding RT Structure Set file of the patient, and (b, c) Photos of the developed phantom incorporating the ion chamber inserts for point dosimetry.

The hollow phantom was subsequently filled with water that served as soft tissue equivalent. All ten treatment plans were created in the Monaco TPS (ELEKTA Instrument, AB, Stockholm, Sweden). It was crucial to deliver the treatment plan prepared using the actual patient's CT dataset to the developed patient-specific phantom, without the recalculation of the plan on the phantom CT image series, and directly compare measurements with the calculated dose distribution in the actual patient's anatomy. Each phantom was irradiated using the specific patient's irradiation protocol including the image guidance radiation therapy (IGRT) step.

Therefore, the patient-derived plan was transferred to MOSAIQ and then imported to XVI for preparation. The phantom was set up on the robotic couch with the corresponding patient's thermoplastic mask on the SRS base plate (Figure 3). The isocenter was confirmed and the registration clip-box was set to cover the entire skull. An XVI VolumeView cone-beam CT scan was then performed, with the ion chamber in-place, and the resulting reconstructed images were co-registered with the patient CT images in the TPS to accurately define ionization chamber positions (Figure 4). The detector's sensitive volume was identified and delineated. Corrections were made in 6D, and the translations and rotations provided were executed by the HexaPOD robotic couch. All treatments were then delivered by an ELEKTA VersaHD 6/10 MV or Axesse 6 MV linear accelerator. Mean values of the ionization chamber's sensitive volume from the TPS calculations in the patient anatomy were compared with the corresponding measurements (Figure 5).

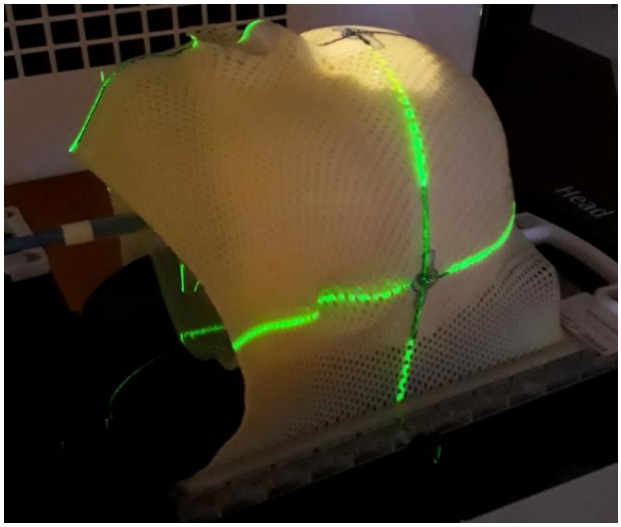

Figure 3. Phantom setup on the treatment couch with the actual patient's thermoplastic mask on the SRS base plate.

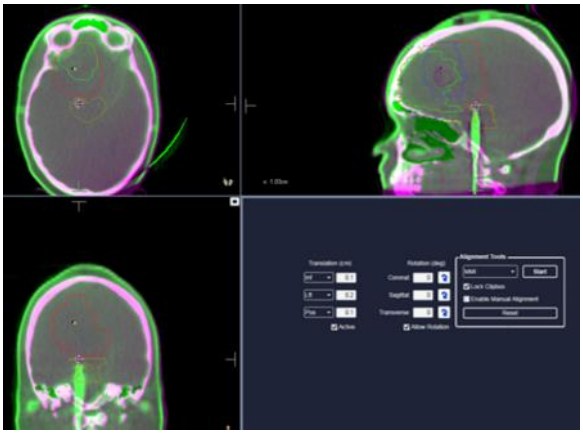

Figure 4. Cone-beam CT scan of the personalized phantom registered on the real patient's CT images during the IGRT step for a glioblastoma case.

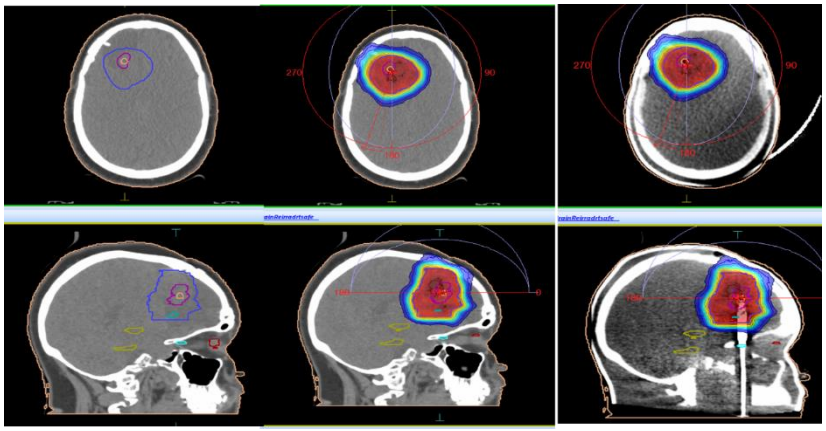

Figure 5. Contours (left) and dose distributions (middle) on patient CT images, co-registered with corresponding phantom CBCT images (right) to derive the expected chamber dose values.

Overall 16 PTVs and 21 OARs were evaluated. Box plots in Figure 6 summarize the distribution of percentage difference between ion chamber measurements and corresponding TPS calculations in the patient anatomy for both PTVs and OARs.

Regarding the PTVs, an overall excellent agreement between measurements and calculations is noticed. A general underestimation of ion chamber measurements with respect to TPS calculations is observed, with median percentage difference from TPS calculations of the order of -2.9% ± 2.0%. All differences lie within ±4.0%, in the low dose gradient/high dose region within PTV, complying with general recommendations regarding the overall accuracy in the radiation dose delivered to the patient dose specification point, of ±5-6% of prescription dose at the 95% confidence level[12,13].

In the OARs region, the degree of agreement between measurements and calculations strongly depends on the defined accuracy of the position of the ionization chamber sensitive volume in the patient anatomy, as well as, on the dose gradient in the region of measurement resulting in increased differences in the high dose gradient regions. As shown in the right boxplot of Figure 6, percentage difference between ion chamber measurements and corresponding TPS calculations present a wide distribution. Ion chamber deviations show a median overestimation of the order of 3.3% ± 10.6%, presenting however a large dispersion, where difference reaches up to 17.8%. In any case, differences of the sample's interquartile range remain within ±10%, complying with the failure modes and effects analysis (FMEA) proposed by TG-100[14], regarding the failure in the delivery accuracy of the dose distribution. Moreover, the measured dose delivered to all OARs of this study, is always lower than the accepted dose limit for the specific OAR with respect to the fractionation scheme used.

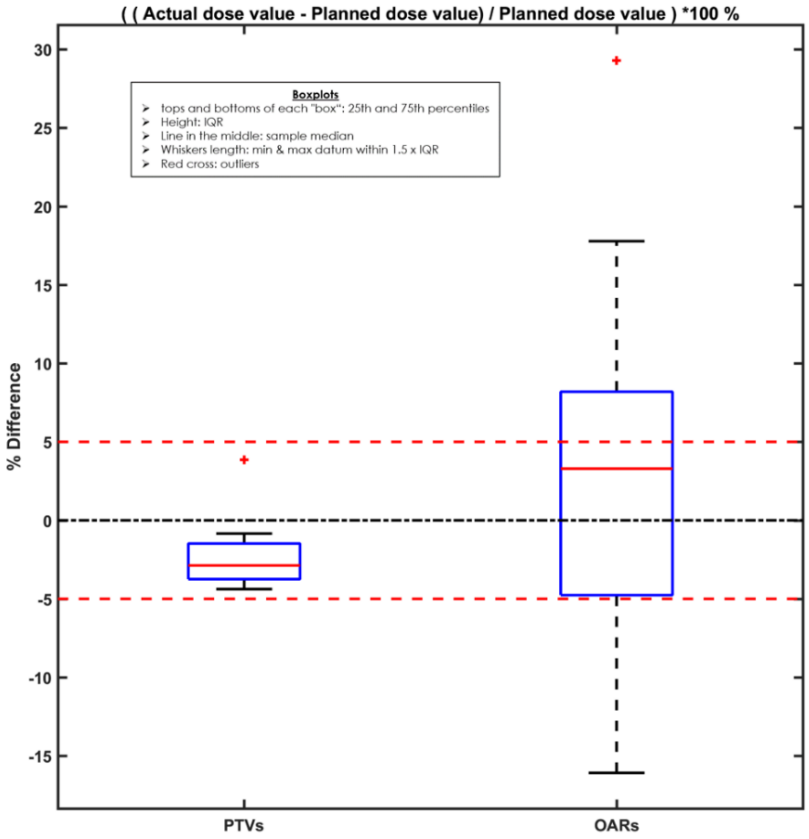

Figure 6. Results of the comparison of ion chamber measurements with corresponding TPS calculations in the patient anatomy for both PTVs and OARs. The red dashed horizontal lines mark the recommendation for accuracy in the radiation dose delivery of ±5%[12–14].

While ion chamber dosimetry remains the gold standard for point dose measurements, due to the widely accepted advantages it presents[15], there are well known limiting factors in using ionization chambers in SRS/SRT, IMRT and VMAT treatments where small fields or small beamlets might be involved. These limiting factors are mostly related to their sensitive volume size and the lateral electronic disequilibrium effects[16–18] and result in an underestimating response[19] at in-field measurements and overestimating at the penumbra region[20,21]. This under-/overestimation was also confirmed by the results of this study in the measurements within PTVs and OARs, respectively. However, these limitations are overcome by applying the appropriate correction factors depending on the specific detector-case[22]. In this study, the maximum difference found was of the order of 29% in a brainstem OAR, however, even in this worst-case scenario the total dose was still 40% lower than the tolerance dose of the specific OAR with respect to the fractionation scheme used, lying on the safe side. In charged particle disequilibrium conditions, no optimal detector exists for dose measurements. The smallest perturbation seems to be achieved with films. PPP is also designed to incorporate a film dosimetry insert made of water equivalent material for absolute and relative 2D dosimetry in two different orientations; sagittal or coronal plane, depending on the user's needs.

Evidence-based confidence

A novel literally patient-specific end-to-end QA methodology for dose verification in advanced radiotherapy applications is presented and evaluated. Using the Personalized PseudoPatient™, dose measurements are performed directly within selected PTVs and OARs of the real patient's replicated anatomy, using the department's ion chambers or films, enabling the confirmation that the TPS calculated dose is actually delivered with dosimetric and geometric accuracy in an absolutely personalized way. More specifically, overall results of this work suggest that the implemented methodology based on 3D-printing technology is capable to verify the dose in clinically significant regions within the patient, by delivering the exact same plan intended for the patient, without the need of plan recalculation in the phantom anatomy. The RTsafe truly personalized pre-treatment plan verification concept successfully addresses the challenges of the first fraction of the radiotherapy course, through a complete treatment process chain check that assesses all possible involved accuracy and uncertainty considerations. Personalized PseudoPatient™ provides to the medical treatment team and each patient separately the peace of mind that the treatment will be delivered as planned, in an efficient and safe way without the risk to compromise the treatment outcome. The measurements performed can be used for the patients' medical record and for insurance companies' requirements.

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