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Original paper

High resolution ion chamber array delivery quality assurance for robotic radiosurgery: Commissioning and validation

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ABSTRACT

Purpose: High precision radiosurgery demands comprehensive delivery-quality-assurance techniques. The use of a liquid-filled ion-chamber-array for robotic-radiosurgery delivery-quality-assurance was investigated and validated using several test scenarios and routine patient plans.

Methods and material: Preliminary evaluation consisted of beam profile validation and analysis of source–detector-distance and beam-incidence-angle response dependence. The delivery-quality-assurance analysis is performed in four steps: (1) Array-to-plan registration, (2) Evaluation with standard Gamma-Index criteria (local-dose-difference $\leqslant$ 2%, distance-to-agreement $\leqslant$ 2 mm, pass-rate $\geqslant$ 90%), (3) Dose profile alignment and dose distribution shift until maximum pass-rate is found, and (4) Final evaluation with 1 mm distance-to-agreement criterion. Test scenarios consisted of intended phantom misalignments, dose miscalibrations, and undelivered Monitor Units. Preliminary method validation was performed on 55 clinical plans in five institutions.

Results: The 1000SRS profile measurements showed sufficient agreement compared with a microDiamond detector for all collimator sizes. The relative response changes can be up to 2.2% per 10 cm source–detector-distance change, but remains within 1% for the clinically relevant source–detector-distance range. Planned and measured dose under different beam-incidence-angles showed deviations below 1% for angles between 0° and 80°. Small-intended errors were detected by 1 mm distance-to-agreement criterion while 2 mm criteria failed to reveal some of these deviations. All analyzed delivery-quality-assurance clinical patient plans were within our tight tolerance criteria.

Conclusion: We demonstrated that a high-resolution liquid-filled ion-chamber-array can be suitable for robotic radiosurgery delivery-quality-assurance and that small errors can be detected with tight distance-to-agreement criterion. Further improvement may come from beam specific correction for incidence angle and source–detector-distance response.

1. Introduction

Comprehensive delivery quality assurance (DQA) is required for high-dose radiosurgery to ensure accurate treatment delivery and hence patient safety. Accurate and sensitive dosimetric methods and detailed procedures are needed both in daily routine QA and

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for patient-specific DQA especially when frameless image-guided radiosurgery is delivered by complex systems such as the robotically steered CyberKnife® (Accuray Incorporated, USA) [1,2]. The CyberKnife uses registration of stereoscopic X-ray images to the planning computer tomography (CT) to locate and position the patient on the treatment couch. Patient position shifts in reference to the calibrated imaging center are tracked and corrected by the robot. Inverse treatment planning is based on sequential multi-objective optimization, which generally results in an arrangement of several non-isocentric non-coplanar beams of various sizes and source–detector-distances (SDDs) generating complex dose distributions with steep dose gradients. Commissioning and performance testing of the CyberKnife have been widely reported [3–5] and the quality assurance necessary for robotic radiosurgery was summarized in the American Association of Physicists in Medicine (AAPM) Task Group 135 report [6].

Radiochromic film measurement is the current method of choice both for routine QA as well as specific validation of patient treatment plans for the CyberKnife [6,7]. The commissioning and validation for film based CyberKnife DQA using various test scenarios [7] was recently reported and results confirmed that, by means of accurate film-to-plan registration, maximum Gamma-Index pass-rate search and tight distance-to-agreement (DTA) criteria, small errors in beam delivery and system miscalibration can be detected. However, some drawbacks of film based methods applied to CyberKnife, remained unsolved: (1) absolute film dosimetry requires additional ion-chamber verification and appears to have an accuracy of no less than 3% [7] and (2) film DQA evaluation is cumbersome and requires long wait times (up to several hours) after irradiation. The generally long times required both to perform and analyze patient specific film DQA may significantly reduce the number of dosimetrically verified clinical treatment plans.

On the other hand, DQA for conventional linear accelerators with Multi Leaf Collimators (MLC) is routinely performed using two-dimensional ion-chamber or diode arrays [8–11]. However, the diode or chamber spacing of these arrays (0.5–1.0 mm) is generally too large for the small CyberKnife beams. Recently, a new high-resolution liquid-filled ion-chamber array (Octavius1000SRS, PTW, Germany) with 2.5 mm chamber spacing at the center was developed purposefully for small field radiosurgery DQA. The general dosimetric properties of the 1000SRS are promising [12,13], but specific questions regarding angular and dose-per-pulse (DPP) dependences [14] originating from small non-coplanar beams with variable SDD remain unanswered for the applicability to CyberKnife DQA. Specifically, the following questions need to be addressed before validating CyberKnife treatment plans using the 1000SRS:

(1) Is the 1000SRS chamber spacing (2.5 mm at the center) appropriately sensitive for the small field sizes of the CyberKnife (5–60 mm)?
(2) Does the DPP and thus SDD dependence of the 1000SRS influence the DQA measurements for clinical CyberKnife plans with variable SDDs (typically 80–90 cm)? Liquid filled ion-chambers are subject to much larger recombination effects [14]. Specifically, the volumetric recombination, which refers to the recombination of two ions coming from different ionization events, are dependent on dose rate and therefore on the distance of the beam source and the detector [14].
(3) Are the different incident angles of a CyberKnife plan (typically 0–110°) influencing the DQA measurements performed using the 1000SRS? Array dose responses are generally dependent on beam incidence angle, especially for lateral beams passing through multiple diodes or chambers. Various techniques such as synchronously rotating the array or using angle correction factors [15,16] have been implemented in clinical routine. However, rotating the 1000SRS synchronously with the CyberKnife is non-trivial due to the six degrees of freedom of the robot.

In this study, a streamlined CyberKnife DQA process using the Octavius 1000SRS detector was developed and evaluated. The design of the study followed the scheme we had previously implemented for film based DQA [7]. The test scenarios proposed for film dosimetry were used with minor modifications to evaluate the sensitivity of the proposed 1000SRS DQA method to system delivery errors and geometric misalignments. A benchmark will be established for commissioning liquid-filled ion-chamber array-based CyberKnife DQA and the results will be compared against the current gold standard (film). Furthermore, new tests were added to address the specific issues related to the use of the array, such as DPP and angular dependence. The appropriate criteria for Gamma-Index analysis were also evaluated in reference to our previous findings with film DQA [7] and the proposed tolerance levels were validated on a large number of clinical treatment plans in multiple institutions.

2. Methods and materials

2.1. High-resolution liquid-filled ion-chamber array

The Octavius 1000SRS detector array consists of 977 MicroLion liquid-filled ionization chambers that are arranged in a square plane. The chamber has a sensitive volume of 2 mm^3 and is filled with iso-octane having a density of 0.688 g/cm^3. The size of each detector is 2.3 × 2.3 × 0.5 mm (2.65 mm^3) and the spacing in the high resolution inner area (5.5 × 5.5 cm^2) is 2.5 mm (center to center), whereas the spacing of the detector in low resolution outer area (up to the full 11 × 11 cm^2 measurement area) is 5 mm (center to center). The properties and characteristics of the 1000SRS have been thoroughly investigated for conventional linear accelerators [12,13].

2.2. Dosimetric analysis of the 1000SRS specific for CyberKnife DQA

To assess the sampling distance and resolution, the *x* and *y* profiles of the 12 collimated small circular CyberKnife beams (5, 7.5, 10, 12.5, 15, 20, 25, 30, 35, 40, 50, 60 mm) were measured with the 1000SRS and compared to profiles measured in a water phantom using a synthetic diamond detector (TM60019, PTW), which was previously evaluated and validated for accurate CyberKnife beam commissioning [17]. The TM60019 has a sensitive volume of 0.004 mm^3. The water phantom axis and the 1000SRS array were positioned along the CyberKnife robotic coordinate system. The TM60019 detector was aligned to the center of the field and positioned orthogonal to the beam direction. The *x* and *y* profiles were measured at 5 cm water depth and a source–surface-distance of 80 cm. The 1000SRS measurements were performed in water equivalent RW3 (PTW) in the same setup. The output factors measured with the 1000SRS were compared to measurements with the TM60019 and with the small field diode E (TM60017, PTW). The output factors for the TM60019 were uncorrected as the TM60019 appears to require only small corrections relative to dose in water [17] and the output factors for the TM60017 were corrected by using Monte Carlo factors according to [18].

To assess the SDD response variability the array central chamber was cross-calibrated in dose-to-water against a reference SemiFlex 0.125 cm^3 ion-chamber (PTW) using the 60 mm collimator and varying the SDD from 60 cm to 120 cm, both for the chamber and the array. The phantom build-up configurations varied

from center to center (1–3 cm), but were always the same for the measurements performed in the same center. Additionally, the SDD dependence curves were also converted in a DPP response curves using the center specific pulse repetition frequency (PRF) and dose rate values and compared to previous publications [12].

To analyze the angular response we evaluated the reading of the central chamber of the 1000SRS for each possible beam direction (node) of an isocentric treatment plan and compared the measurement to the standard treatment planning dose calculation (Ray Tracing) for that beam.

2.3. Gamma Index analysis

Gamma-Index analysis was performed using VeriSoft (Version 6.1, PTW). The acceptance ellipsoid was defined by considering the local percentage dose difference (LDD) and the distance-to-agreement (DTA) criteria. In the following, we will simplify each used combination as *X*%/*Y* mm where *X* indicates the LDD in percent and *Y* the DTA in mm. Since the 1000SRS measurement area is larger (11×11 cm) than the commonly used radiochromic CyberKnife films (6×6 cm), we were able to increase the analyzed dose levels from 50–100% to 20–100% as compared to our previous work [7].

2.4. Array-based delivery quality assurance

For the DQA of clinical patient treatment plans, we projected the beam arrangement onto the 1000SRS. The array was used adding 1–3 cm RW3 build-up material that included a 1 cm RW3 thick gold fiducial marker plate (PTW) screwed to the 1000SRS for accurate CyberKnife X-ray image guidance. For dose calculation, the 1000SRS together with build-up was set to RW3 equivalent electron density (1.03 g/cm^3 [13]) in the phantom CT scan setting. The remaining part of the image was assumed to consist of air equivalent electron density to compensate for CT artifacts from the electronics. We recalculated the dose distribution for the phantom plan using the standard RayTrace dose calculation algorithm.

Since VeriSoft assumes the central chamber to be coincident with the dose calculation grid center, array-to-plan registration was performed by aligning the center of the dose calculation box to the central ion-chamber of the 1000SRS. The registration was performed manually for each plan and visually checked using the 1000SRS phantom CT. The geometric accuracy and reproducibility of the whole procedure is approximately 0.5 mm, thus larger than the one achievable with film based methods [7].

Since a beam by beam angle and SDD correction is not yet possible in either VeriSoft or in the CyberKnife planning system we were only able to correct the 1000SRS measurement by applying an average beam SDD correction factor as determined during cross-calibration.

For plan DQA evaluation, we adopted the following three-step procedure from the previously published film-based DQA method [7]:

(1) A preliminary comparison of the delivered and planned dose distributions is performed after array-to-plan registration using initially the 2%/2 mm 3D Gamma-Index criteria and requiring a pass-rate above 90% according to the AAPM TG 135 [6]. We use the 3D Gamma-Index analysis due to uncertainties in measurement plane definition on the phantom CT.
(2) The contour-matching-based auto alignment function of VeriSoft is used first in-plane in combination with the Max_γ search [7] second out-of-plane to determine the displacement vector which optimizes the Gamma-Index passing rate. The maximum displacement tolerance was set to 1.5 mm, which includes the global beam delivery and array-to-plan registration uncertainties.
(3) The required final tolerance was a pass-rate above 90% using 3%/1 mm for 2D Gamma-Index analysis. In order to evaluate the limitations of the method, we also computed Gamma-Index pass-rates for 2%/1 mm criteria.

2.5. Sensitivity and reproducibility tests

The first test scenario was designed to study the array sensitivity to translational beam and plan shifts using the VeriSoft auto alignment function. For the beam shift detection, beams with various sizes (5 mm, 35 mm, 60 mm) were vertically centered over the central ion-chamber of the 1000SRS and shifted at 0.1 mm steps in the superior-inferior and left–right direction moving the robot. At each position, 100 Monitor Units (MU) was delivered and compared to the reference un-shifted robot position using the auto alignment function. For the plan shift detection, a standard spherical isocentric CyberKnife End-2-End plan [6] was used. Before plan delivery the phantom was shifted by 0.3, 0.5, 1.0 and 2.0 mm in superior–inferior direction and the results were again compared to the baseline un-shifted plan using the auto alignment function.

The second test scenario was designed to study the reproducibility of beam delivery over time. A single 60 mm beam plan was delivered 25 times over a period of one month including setup re-positioning of the fiducial plate as well as of the liquid-filled ion-chamber array on the treatment couch. The displacement of the beam and the delivered dose were compared to a reference delivery acquired at the beginning. As the 1000SRS absolute dose response is dependent on temperature changes (yet not on pressure changes) the room temperature was monitored and kept constant during the measurements. We also measured and evaluated a clinical plan multiple times at different days.

2.6. Dose miscalibration and missing beams test

The third test scenario was a miscalibration of the system dose output ranging from 0.5% to 5.0% in 0.5% steps. Again, a standard spherical isocentric CyberKnife End-2-End plan [6] was delivered with the clinical calibrated output (reference) and then with the miscalibrated output.

The last test scenario was created to evaluate the sensitivity of Gamma-Index analysis and the related proposed criteria to non-delivered treatment beams. Total MU of 128 (0.8%), and 246 (1.5%), each from a single beam, and 374 (2.3%) from two beams and 490 (3%) from three beams were removed from a complex beam arrangement (total beams 170, total MU 16364). The removed beams were initially pointed at the inferior section of the complex target. The corresponding delivered dose distributions were then compared to the original treatment plan dose calculation. Since this test was performed removing beams, it was expected to yield some variations also in the shape of the delivered dose distribution and thus allowed a sensitivity evaluation to both dose-difference and distance-to-agreement criteria in Gamma-Index analysis. Although the possibility of the CyberKnife treatment system not delivering beams during treatment is remote, the aim of the test was to simulate a gradually increasing difference between delivered and planned dose distributions to analyze the sensitivity of 1000SRS-based DQA method. Similar approaches have previously been reported for different delivery techniques [7,9–11] and for film based DQA procedures [7].

2.7. Clinical patient plans

To validate the method independently 55 routine DQA tests of clinical patient plans were performed in five different clinics with various CyberKnife generations: (a) CyberKnife G3, Saphir Radiosurgery Center Northern Germany, Güstrow, Germany, (b) CyberKnife G4 (VSI), Saphir Radiosurgery Center Frankfurt am Main, Germany, (c) CyberKnife G4, IFCA, Florence, Italy, (d) CyberKnife G4, Greater Poland Cancer Centre, Poznan, Poland and (e) CyberKnife M6 Series, Schwarzwald-Baar-Klinikum, Villingen-Schwenningen, Germany. The phantom CT scan resolution varied among the CyberKnife centers between 0.61 and 0.82 mm (left–right, ant-pos) and 0.68 and 1.00 mm (inf-sup).

2.8. Comparison with film dosimetry

The study design was purposefully adopted following the scheme we previously used for the validation of CyberKnife film DQA [7]. The 1000SRS sensitivity to plan translational shifts, missing beams and dose miscalibration was tested following the same procedures we used to evaluate the sensitivity of film dosimetry [7], thus permitting a direct comparison between the two methods. The evaluation of clinical plans DQA was also performed adopting rigorously the same method and Gamma-Index criteria used for film dosimetry [7], thus enabling a meaningful comparison between the Gamma-Index pass-rates obtained by the 1000SRS and film DQA.

3. Results

3.1. Dosimetric analysis of the 1000SRS specific for CyberKnife DQA

The profile comparison measured with the 1000SRS and the TM60019 showed Gamma-Index pass-rates of 91.9% (x-axis) and 97.0% (y-axis) for 0.5%/0.5 mm criteria and median local percent dose differences of 0.11% (±2.4%, x-axis) and 0.10% (±2.5%, y-axis) for all collimators (Fig. 1) confirming the applicability of the liquid-filled ion-chamber array for the small CyberKnife beams. The measured output factors with various CyberKnife systems show an overall sufficient agreement (Fig. 2). The difference between 1000SRS and TM60019 and TM60017 (Monte Carlo corrected according to [18]) for 7.5 mm and 5 mm collimator was in the order of 1.5% and 3.0%, respectively, agreeing well with previous publications on CyberKnife output factors [14,17,18]. As the dose-per-pulse effect with smaller fields is in the order of 0.35% [14] volume averaging effects in the 1000 SRS would probably be responsible for the 3% under-response for the 5 mm collimator output factor and warrant further investigation.

The dose response measurements at various SDD confirm the DPP dependence of the 1000SRS and clinical correction factors normalized at the nominal reference distance of 80 cm are shown for the different detectors and CyberKnife (Fig. 3). Due to different PRF and dose rates, the DPP value at 80 cm SDD is different from center to center, but is consistent with different 1000SRS detectors. It is essential to remark, that although the variability among the calibration factors is large over the entire SDD range, between 80 and 90 cm SDD, which corresponds to the majority of beams in clinical treatment plans, the SDD dependence is within 1% for all considered CyberKnife systems and detectors.

Beams with incidence angles over 80 degree (indicated as lateral beams in the following) demonstrated a high local dose difference (>10%) between the 1000SRS central dose measurement and the plan dose calculation (Fig. 4). For angles smaller than 80°, which includes the majority of the CyberKnife beam angles, the differences were generally small (mean local dose difference 0.74%). An average CyberKnife treatment plan has approximately 8% of its MU delivered by lateral beams (see section clinical patient plans) which may result in a total local dose difference of approximately 1.5%. For treatment plans with more relative MU (e.g., 20%) from lateral directions the total local dose difference may potentially raise to 3.0%, which needs to be considered when analyzing the DQA measurements.

3.2. Sensitivity and reproducibility tests

The 0.1 mm beam shifts introduced by moving the robot were detected using the auto alignment function with an accuracy of 0.03 mm (mean absolute accuracy 0.01 mm in superior-inferior and 0.02 mm in left–right direction) for various collimators. The End-2-End plan shifts were detected by the auto alignment function with an accuracy of 0.15 mm (Table 1). The Gamma-Index analysis performed before auto alignment with 2%/2 mm criteria did not detect any shift (pass-rate < 90%) while 3%/1 mm criteria yielded a pass-rate <90% only for the 1 mm and 2 mm shifts. The sensitivity to translational shifts obtained by this test for the 1000SRS using the VeriSoft auto-alignment software was consistent with previous reported results obtained by film dosimetry applying the Max_γ search method [7], which showed an accuracy of 0.3 mm.

Repeating the beam delivery 25 times resulted in a mean and maximum displacement to reference of 0.07 mm and 0.22 mm (left–right) and 0.20 mm and 0.34 mm (inf–sup). The mean and maximum displacement to reference measured with film (Daily Automated Quality Assurance Test [6]) in the same time period was 0.09 mm and 0.24 mm (left–right) and 0.15 mm and 0.37 mm (inf–sup) matching the results of the 1000SRS within

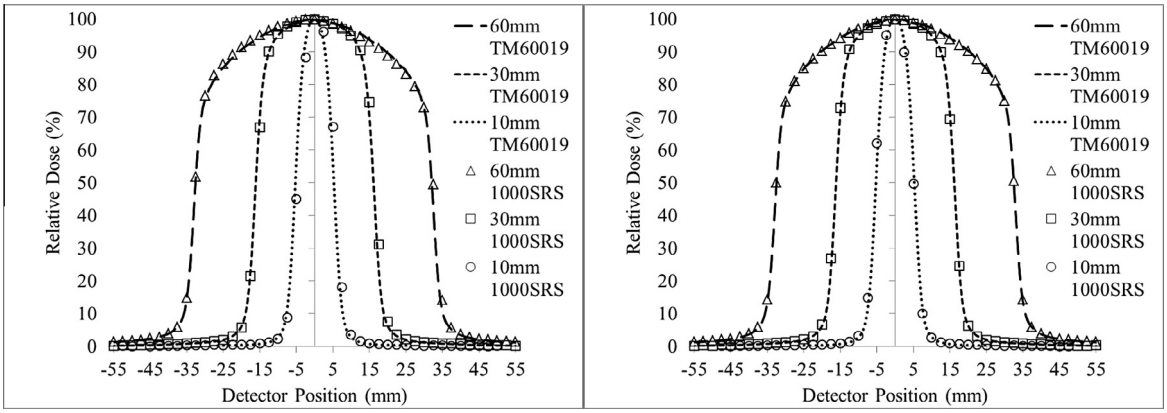

Figure 1. Profile measurements along the robotic x (left) and y (right) axis with the 1000SRS and the TM60019 with the 10 mm, 30 mm and 60 mm collimator.

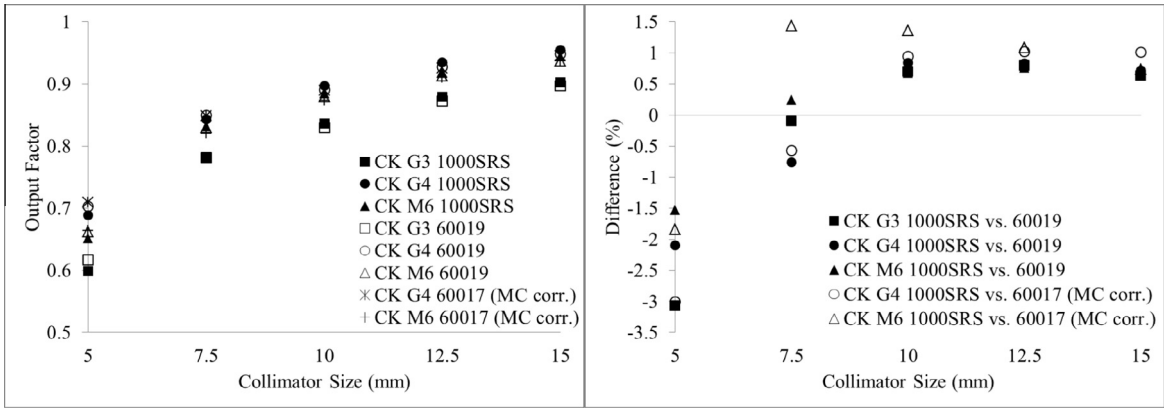

Figure 2. Left: Output factors for the small CyberKnife (CK) fields measured by 1000SRS, TM60017 (diode E) and TM60019 (microDiamond). Right: Difference between the various output factors. The output factors for the TM60019 were uncorrected [17] and the output factors for the TM60017 were corrected for using Monte Carlo factors according to [18].

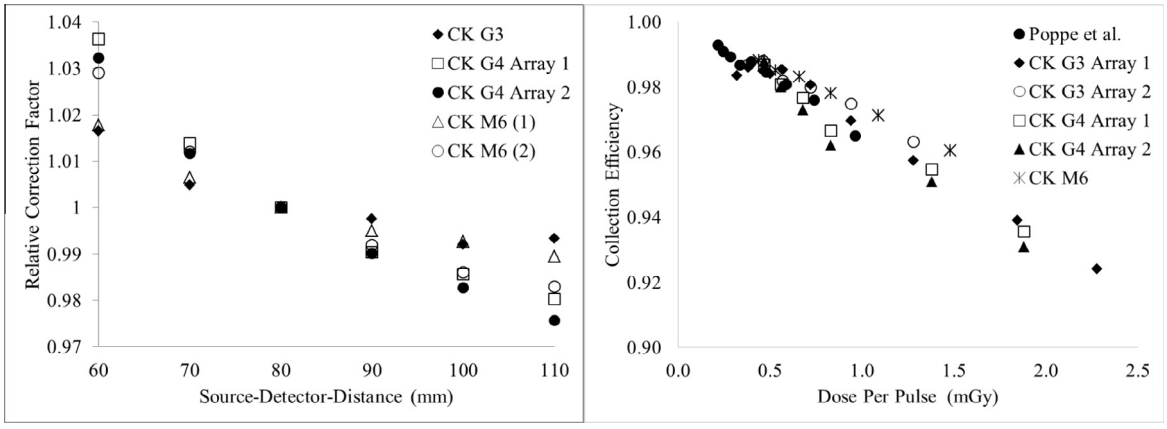

Figure 3. Left: relative calibration factors of the 1000SRS at various source–detector-distances (SDDs). The dose per pulse (DPP) at 80 cm SDD for the CyberKnife (CK) G3 was 0.72 mGy/pulse, for the CK G4 1.06 mGy/pulse and for the CK M6 0.83 mGy/pulse. Right: DPP dependence for various CK and arrays in comparison to Poppe et al. [12].

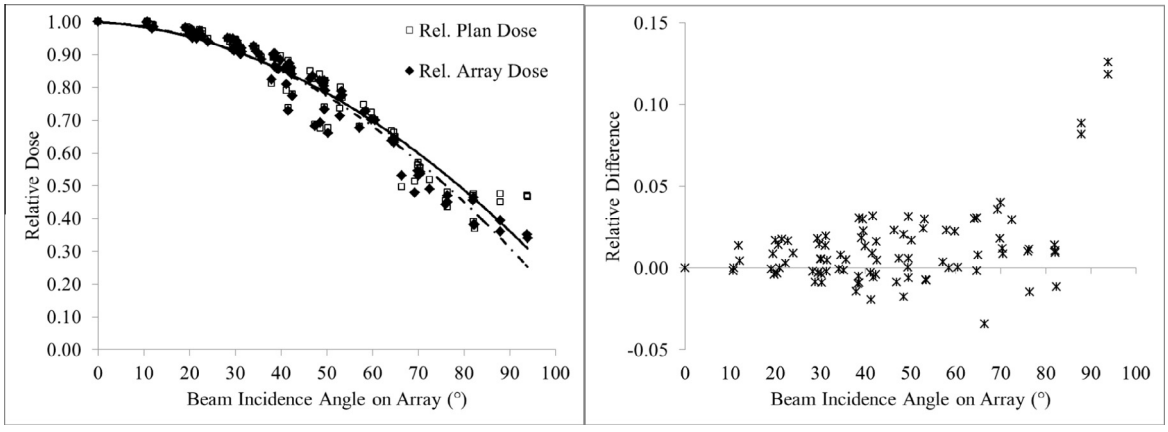

Figure 4. Beam incidence angle response for an iso-centric treatment plan with 60 mm collimator. Left: relative dose of dose calculation and array measurement (lines indicate a polynomial fit function). Right: relative difference of the dose calculation and the measurement.

0.05 mm. The measured mean dose difference to baseline was 0.18% for the 1000SRS with temperature control and 0.15% for a reference ion-chamber (T30012, PTW) used for daily dose measurements in the same time period. Repeating the delivery and evaluation of a clinical plan at different times, the difference was <3.0% in Gamma-Index pass-rate for both 3%/1 mm and 2%/1 mm criteria, which is in agreement with published literature [12,13].

3.3. Dose miscalibration and missing beams test

The analysis with various Gamma-Index criteria of the introduced system absolute dose miscalibrations is summarized in Fig. 5. Gamma-Index analysis with 2%/2 mm criteria did not indicate any miscalibrations <4% while 1%, 2% and 3% local dose difference with 1 mm distance to agreement detected 2.0%, 2.5% and

Table 1
Gamma analysis of End-2-End plans shifted before delivery.

1000SRS Shift	Before alignment Gamma pass-rate		Auto alignment	
S/I (mm)	2%/2 mm %	3%/1 mm %	*L/R* (mm)	*S/I* (mm)
−0.30	100.00	100.00	−0.02	−0.35
−0.50	100.00	100.00	0.00	−0.49
−1.00	100.00	76.50	0.00	−1.15
−2.00	92.50	38.50	0.00	−2.00

S/I = Superior/Inferior, *L/R* = Left/Right.

3.5% miscalibrations. Gamma-Index analysis with 2%/1 mm was found to be the most sensitive criteria (steepest slope) for system absolute dose miscalibration detection for our test scenario.

The analysis performed for increasing number of missing beams during plan delivery is summarized in Table 2. The Gamma-Index analysis with 2%/2 mm detected missing MU above 1.5% (pass-rate < 90%) while the 3%/1 mm criteria after auto alignment indicated missing MU above 0.8%. However, as the test scenario had a complex dose distribution with a high number of lateral beams (compare Fig. 6) the reference pass-rate with 3%/1 mm was already low (90.1%) and 2%/1 mm could not be used as criteria, yielding a passing rate below 90% already for the reference delivery. Furthermore, with higher missing MU during plan delivery the auto alignment function also showed larger shifts due to the changes in the measured isodose lines. Nevertheless, the drop in pass-rate was the steepest for 3%/1 mm Gamma-Index criteria. The results confirmed what was reported for film dosimetry with a similar test: film showed the higher sensitivity to this test using 1 mm DTA, while the 2%/2 mm criteria could only detect higher differences (5%) [7].

3.4. Clinical patient plans

The DQA results of clinical patient plans are summarized in Table 3. Before analysis, a center specific average SDD correction factor was applied to each measurement, as specified in the materials and method section. After array-to-plan registration, 2%/2 mm Gamma-Index analysis yielded pass-rates above 90% for 54 out of 55 cases, where a non-optimal registration may have been the cause for failure in the remaining case. Performing auto alignment and Max$_\gamma$ search, we obtained shifts <1.5 mm (mean absolute, 0.48 mm) in all cases. Final results yielded 3%/1 mm pass-rates above 90% (mean, 95.8%) for all cases. Gamma-Index analysis with 2%/1 mm yielded pass-rates above 90% (mean, 90.8%) for 30 out of

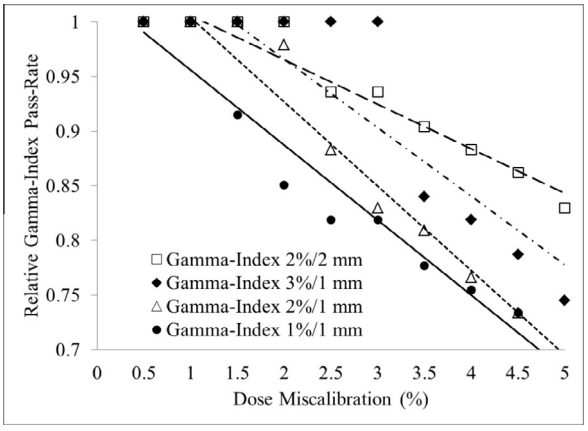

Figure 5. Gamma analysis of various absolute dose miscalibration tests (lines indicate a linear fit function for each of the data sets).

Table 2
Gamma analysis with and without missing the delivery of beams.

Missing	Before alignment			After alignment	
	Gamma pass-rate	Auto alignment		Gamma pass-rate	
MU (%)	2%/2 mm %	*L/R* (mm)	*S/I* (mm)	3%/1 mm %	2%/1 mm %
0.00	94.30	−0.65	0.64	90.10	80.10
0.80	93.40	−0.80	0.84	86.10	79.10
1.50	83.40	−0.55	1.05	72.50	67.40
2.30	79.60	−0.65	1.14	67.30	63.00
3.00	79.10	−0.69	1.10	66.40	62.20

MU = Monitor Units, *S/I* = Superior/Inferior, *L/R* = Left/Right.

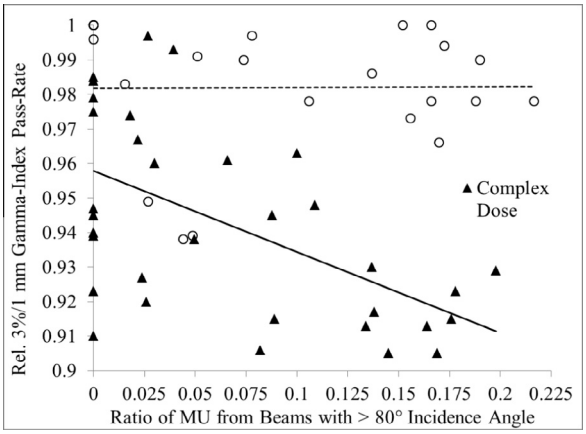

Figure 6. 3%/1 mm Gamma-Index pass-rate after alignment as a function of ratio of lateral beams divided into complex shaped (black triangles) and spherical shaped (open circles) dose distributions (lines indicate a linear fit function for each of the data sets).

55 cases (54.5%) and above 80% for 54 out of 55 cases (98.2%). It may be noted that for some cases the pass-rate for 2D Gamma and 2%/1 mm criteria is higher than for 3D Gamma and 2%/2 mm, which is again caused by non-optimal registration. Data previously obtained for film dosimetry on a similar sample (33 plans) [7] yielded slightly lower passing rates. For 3%/1 mm the film Gamma-Index pass rate was above 90% in only 83% of cases (mean 94.5%). It must be highlighted that the isodose threshold used for film analysis was 50% due to the limited dimensions of the phantom, as compared to a 20% threshold adopted in the present work.

The pass-rates seem to be independent of location (head or body), number of beams, collimator sizes, maximum doses, or performing CyberKnife center. The pass-rates for the extracranial cases were however strongly influenced by adding the average SDD correction factor (mean pass-rate 87.9% without versus 93.3% with average SDD correction factor) when the CyberKnife showed stronger DPP dependencies (CyberKnife G4, compare Fig. 3). At first sight, the pass-rates also seem to be not influenced by the percentage of MU delivered from lateral beams (incidence angle above 80°). However, considering the complexity of the dose distribution (spherical versus complex shape), a trend towards lower pass-rates with increasing percent MU from lateral beams can be observed for complex shaped but not for spherical dose distributions (Fig. 6).

4. Discussion

Quality assurance (QA) using radiochromic film is routine practice for robotic radiosurgery [5–7]. Absolute film dosimetry for CyberKnife delivery quality assurance has been shown to yield

Table 3
Gamma analysis of routine patient plans.

No.	Location	Beams	Collimator	Max	3D Gamma	Auto alignment		Max (γ)	2D Gamma		Angle >80°	Mean SDD
				Dose	2%/2 mm	*L*/*R*	*S*/*I*	*A*/*P*	3%/1 mm	2%/1 mm		
			(mm)	(cGy)	(%)	(mm)	(mm)	(mm)	(%)	(%)	(% MU)	(cm)
1	Body	202	15, 25, 35	989	99.9	−0.08	0.14	0.00	99.3	96.5	4.0	90.9
2	Body	147	10, 20, 30	1503	97.8	−0.31	1.12	0.68	94.7	88.5	0.0	89.3
3	Body	156	12.5, 20	1530	94.8	0.88	1.30	−0.68	98.3	92.2	1.6	91.0
4	Body	171	15, 20	1798	95.8	0.27	−0.45	−1.36	93.9	86.1	0.0	89.3
5	Body	160	15, 30, 40	616	85.9	0.67	−1.00	−1.36	96.3	88.4	10.0	91.2
6	Body	141	15, 25	886	97.4	−0.15	−0.83	0.00	97.9	90.7	0.0	89.4
7	Body	113	20, 30	1371	94.7	0.49	−0.83	−0.68	93.8	85.3	5.0	89.8
8	Body	132	10, 15, 25	1756	93.3	0.30	0.20	−1.36	92.3	81.0	0.0	89.6
9	Body	188	10, 20, 30	2171	99.1	−0.31	−0.61	0.00	96.7	90.1	2.2	89.1
10	Body	149	12.5, 25	1362	97.8	−0.05	0.57	0.00	94.5	84.8	0.0	91.0
11	Body	186	15, 35	1591	91.3	0.13	1.20	−0.68	97.4	88.4	1.8	89.5
12	Body	175	25, 50	1195	91.4	0.19	0.41	1.36	98.5	92.0	0.0	90.7
13	Body	168	10, 20, 35	1107	95.0	−1.07	0.23	0.00	91.0	84.3	0.0	89.3
14	Body	151	7.5, 15, 25	1164	96.5	−0.31	0.21	−0.68	92.7	91.3	2.4	89.3
15	Body	166	20	2438	96.7	−0.86	1.41	−0.68	99.7	98.7	7.8	89.2
16	Head	142	10, 20	1274	95.7	1.44	0.01	0.00	90.6	83.7	8.2	83.5
17	Head	120	12.5, 20	833	93.9	0.17	1.10	−0.68	93.9	82.7	4.9	80.6
18	Head	106	15, 20	1802	96.0	0.00	0.00	−0.68	94.9	87.5	2.7	84.7
19	Body	169	20, 35	3092	100.0	−0.54	0.50	−1.22	100.0	99.5	0.0	89.2
20	Body	144	40	1810	97.5	−0.65	0.26	−1.22	99.1	96.9	5.1	89.9
21	Body	133	25	1282	99.5	−0.62	0.29	−1.22	99.7	98.1	2.7	89.5
22	Body	143	15	2624	97.4	0.23	0.25	−0.61	94.8	87.5	10.9	90.2
23	Body	123	15, 25	1843	94.0	−0.92	0.34	−1.22	91.3	85.3	13.4	89.1
24	Body	101	20, 35	3959	95.3	0.26	0.22	0.61	90.5	84.6	14.5	90.9
25	Body	73	35	3564	98.7	0.26	−0.91	0.61	93.8	92.4	4.4	91.9
26	Body	133	12.5, 25	1905	96.3	−0.61	0.88	−1.22	94.0	88.9	0.0	89.8
27	Body	168	20, 35	1310	94.9	−0.37	0.96	−0.61	92.0	86.6	2.6	90.7
28	Body	41	20	2563	100.0	0.13	0.19	0.00	99.0	90.1	7.4	94.1
29	Body	39	20	2867	100.0	−0.81	0.37	−1.22	100.0	97.1	0.0	92.2
30	Body	56	25	3195	97.8	−0.39	0.50	0.00	97.8	86.2	10.6	90.5
31	Body	160	30, 40	2799	90.9	−0.85	0.75	−1.22	96.0	91.0	3.0	92.1
32	Body	150	20	2796	98.5	−0.45	−0.21	0.00	94.5	90.7	8.8	90.5
33	Body	136	20, 35	3932	94.3	−0.81	1.01	−1.22	96.1	92.8	6.6	90.8
34	Body	75	35	4522	100.0	−0.05	0.25	0.00	100.0	99.7	0.0	92.4
35	Body	131	40	3880	99.8	0.24	0.53	0.61	97.5	91.3	0.0	90.7
36	Head	144	10, 15	2508	100.0	−0.22	−0.04	0.00	99.4	99.4	17.2	79.8
37	Head	199	7.5, 12.5	1801	98.9	0.33	0.11	0.00	97.8	98.6	18.8	80.4
38	Head	151	12.5, 25	883	96.6	−0.13	0.31	0.00	90.5	82.5	16.9	82.9
39	Head	166	7.5, 12.5, 20	744	99.6	−0.59	0.37	0.86	97.8	96.0	21.7	80.7
40	Head	117	7.5, 15	2829	100.0	0.29	0.09	0.86	100.0	100.0	16.6	80.7
41	Head	133	5, 20	582	100.0	0.23	0.16	0.00	98.6	97.8	13.7	80.1
42	Head	174	7.5, 12.5	3095	100.0	0.57	0.07	0.86	100.0	100.0	15.2	81.1
43	Head	211	15, 30	694	98.7	0.20	0.31	0.00	97.8	95.0	16.6	81.4
44	Head	183	10, 15	2585	100.0	0.24	0.38	0.86	99.0	96.9	19.0	84.4
45	Head	189	5, 7.5	590	97.5	0.05	0.89	0.00	91.5	89.1	8.9	79.7
46	Body	150	25, 35, 50	2953	93.6	0.63	−0.11	0.86	98.4	94.2	0.0	86.8
47	Body	115	20, 30, 40	810	96.3	−0.09	0.07	0.86	91.3	87.4	16.4	85.1
48	Body	162	10, 15, 20	1324	98.6	0.73	0.14	0.86	91.5	87.1	17.6	79.9
49	Body	141	20, 30, 40, 60	1230	93.0	0.77	0.10	0.00	91.7	82.9	13.8	88.1
50	Body	25	20	740	100.0	−0.06	0.09	0.00	97.3	97.3	15.6	91.8
51	Body	93	12.5, 25	1652	99.7	0.24	0.50	0.00	96.6	94.2	17.0	86.4
52	Body	161	20, 30, 40	1272	90.5	0.64	0.15	0.00	92.3	83.2	17.8	88.3
53	Body	136	10, 25	3267	100.0	0.60	0.55	0.00	99.6	98.5	0.0	85.7
54	Body	135	10, 25	633	96.5	0.39	0.13	0.00	93.0	88.7	13.7	82.8
55	Body	151	30, 40, 50, 60	2588	92.1	0.23	0.60	0.86	92.9	75.6	19.8	82.5
Max		211		4522	100.0	1.44	1.41	1.36	100.0	100.0	21.7	94.1
Min		25		582	85.9	−1.07	−1.00	−1.36	90.5	75.6	0.0	79.7
Average		140		1929	96.7	0.01	0.28	−0.16	95.8	90.8	7.9	87.5

MU = Monitor Units, S/I = Superior/Inferior, L/R = Left/Right, A/P = Anterior/Posterior, SDD = source–detector-distance.
2%/2 mm 3D Gamma-Index criteria was used after registration, but before alignment due to uncertainties in measurement plane definition on the phantom CT. 3% and 2%/1 mm 2D Gamma-Index criteria was used after alignment in all three directions to evaluate the agreement of the calculated and measured dose distributions.

adequate sensitivity to most delivery errors especially when using tight DTA criteria (1 mm) [7]. Although the results obtained with films for clinical DQA are encouraging and permit the use of 3%/1 mm Gamma-Index criteria in most cases, film dosimetry remains cumbersome and we highlighted in our previous publication [7] the limitations and uncertainties related to absolute dose calibration and required long waiting times. For verification of dose distributions, generally diode or ion-chamber arrays are used, e.g., for IMRT and VMAT, often in combination with rotating phantoms [11] or angular correction factors to minimize the variation of detector angular response [15,16]. For the CyberKnife with its non-isocentric non-coplanar beam arrangements, the usefulness of planar ion-chamber arrays and cylindrical diode arrays has been recently investigated [20] while rotating phantoms currently do

not exist. Due to the mentioned limitations of radiochromic film and the increasing demand for high quality DQA measurements we evaluated a CyberKnife DQA procedure which we previously developed for film dosimetry [7] using the high resolution Octavius 1000SRS detector. The rationale was to use the same study design adopted for film dosimetry hence permitting a comparison between the two methods. To this purpose, following our previous study we provided a range of test scenarios to commission the CyberKnife DQA method using the 1000SRS array and to estimate the related sensitivity, similar to currently recommended procedures for IMRT and VMAT [8–11].

Preliminarily, we evaluated the dosimetric characteristics of the 1000SRS for the small CyberKnife beams specifically for CyberKnife DQA and found that the measurements both for the profiles and the output factors match the synthetic diamond detector closely, which was previously evaluated for CyberKnife commissioning [15]. Furthermore, we investigated and confirmed in a multi-site context the source–detector-distance (SDD) and dose-per-pulse (DPP) dependence of the 1000SRS array when used for the CyberKnife beams. This has previously been reported for the MicroLion chamber and for the 1000SRS array for other delivery systems [12–14]. Following the results obtained in this study, we highlighted the necessity of acquiring a center specific SDD response curve prior to the clinical use of the array and the use of a SDD dependent cross-calibration factor, considering that the beam SDD can vary during CyberKnife plan delivery. As a first approximation of the SDD response correction, we propose to calculate an average plan SDD value and to apply the corresponding multiplicative correction factor derived from the SDD response curve. A more rigorous approach would require a SDD correction performed on a beam by beam basis, but dedicated software would have to be developed for this purpose to permit the use in clinical routine. It is also interesting to highlight that without an average plan SDD correction factor the results of the extracranial cases for the CyberKnife G4 (compare Fig. 3) would have resulted in a significant reduction in Gamma-Index pass-rate for almost all cases (mean pass-rate 87.9% versus 93.3%, $p < 0.05$). Dose differences due to beam incidence angle were also investigate and we found larger (>10%) differences only with angles greater than 80 °. This is usually a small percentage (average 7.9%, maximum 21.7% for the examined 55 cases) of the CyberKnife beams for most clinical cases. However for the moment it is not possible to give an accurate estimate of the error introduced by the angular dependence for plans which exhibits a not negligible (>10%) percentage of beam angles above 80 °. The possibility however exists for the user to switch off beams corresponding to angles above 80 ° purposefully for DQA, thus delivering for verification a plan slightly modified as compared to the clinical plan, but at the same time removing all uncertainties due to the angular dependence.

Given the uncertainties due to SSD variations and incidence angle response differences we investigated if the previously determined Gamma-Index criteria for robotic radiosurgery film DQA [7] are adequate when using the 1000SRS. The proposed Gamma-Index criteria by the AAPM TG 135 for film based DQA are 2% dose difference (without reference to global or local dose) and 2 mm distance-to-agreement, requiring a pass-rate above 90% [6]. Similar criteria were also used for a recent study involving a planar and a cylindrical array for CyberKnife DQA [20]. However, from our previous analysis performed for film DQA it was demonstrated that with 2%/2 mm criteria small errors during CyberKnife beam delivery remain undetected [7]. It was suggested to use accurate measurement-to-plan registration, local dose difference and distance-to-agreement criteria respectively of 3% and 1 mm to take better into account the CyberKnife geometric accuracy. We critically analyzed the possibility to adopt the same criteria also for 1000SRS DQA, both in preliminary test scenarios and clinical plans.

The test scenarios with intended beam and plan shifts and the reproducibility tests demonstrated a high reliability of the 1000SRS measurements matching the current gold standard (film). Similar to previous findings with film, we were able to demonstrate the advantages of tighter DTA criteria (1 mm rather than 2 mm). The used test cases highlighted that the selection of a tighter DTA enhanced the sensitivity of the DQA method to small delivery errors, such as small shifts or missing beams, which would have been undetected by Gamma-Index analysis with 2 mm DTA. Moreover, compared to what was previously reported for film DQA, the 1000SRS alone was (as expected) able to detect small system absolute dose miscalibration (2%), again with higher sensitivity when using tighter DTA criteria.

Analysis of clinical treatment plans were performed independently at five different CyberKnife centers and confirmed the robustness of the proposed method for application to CyberKnife DQA. A multi-site evaluation emphasizes the strength of the obtained results since it permits to rule out user's dependent errors as well as all possible biases related to the clinical implementation in a single center. For 55 cases over the 5 enrolled centers, the auto alignment and the Max_γ search was within tolerance (shift < 1.5 mm) in all examined DQA deliveries, confirming that 1.5 mm is an adequate tolerance level for the maximum allowed shift due to the combined uncertainties of registration and beam alignment. This is also a confirmation that the dedicated fiducial plate warrants an adequate tracking accuracy. After alignment, all cases yielded pass-rates above 90% for 3%/1 mm and this result was consistent with the previously reported results obtained by film dosimetry on a 30 plans sample [7]. Although 1000SRS and film DQA tests were not performed using the same clinical plans, the size of the two samples (55 and 30), the inclusion of plans created for a variety of treatment sites, and the multi-site context of both studies make a comparison between the two sets of results meaningful. It is interesting also to remark that 98.2% of the cases yielded pass-rates above 80% for 2%/1 mm. These results indicated the possibility to use Gamma-Index criteria that are tighter than those proposed for lower resolution array based CyberKnife DQA [20] and potentially even tighter than the criteria we recently suggested for film based CyberKnife DQA [7], permitting to decrease the dose difference criteria from 3% to 2% with 1 mm DTA. However, due to the uncertainties related to beam angle and DPP dependence, which are only partially corrected for in our method, the adoption of a 2% dose difference criteria requires caution and further investigation. In the DQA analysis, we were able to include lower isodoses, setting the threshold to 20% instead of 50%. This was previously not possible using accurate film dosimetry [7] due to the small dimensions of the dedicated CyberKnife Ball Cube II phantom.

The Gamma-Index pass-rates for the 1000SRS DQA analysis showed a decrease with increasing ratio of lateral beams, however only for complex shaped dose distributions. The effect was practically not visible for spherical dose distribution. This suggests that for standard spherical dose distribution lower local dose difference criteria (i.e., 1–2%) may be used.

Some drawbacks and limitations of the proposed method should be highlighted. Array-to-plan registration is currently not optimal for a precise estimation of the global geometric delivery accuracy. The registration method presented in this work was based on a manual centering of the dose grid on the 1000SRS array CT scan and is expected to have a higher uncertainty compared to film-to-plan registration (0.5 mm vs. 0.2 mm [7]). It was rather cumbersome to manually define the correct measurement plane and the correct location of the central ion-chamber of the array. The possibility of an automatic registration method using well defined landmarks or an artificial phantom CT scan are highly desirable to further decrease the uncertainty in cross-calibration

and array-to-plan registration (e.g., due to CT artefacts), and hence increase the DQA accuracy. A dedicated correction function for the angular dependence applied to lateral beams would also be highly desirable, since it is currently not possible to discern angular response errors in the DQA results. Similarly, the results of 1000SRS based DQA may be further improved by applying a beam by beam SDD correction during dose calculation instead of an average correction factor, which is under current investigation. Due to those remaining unsolved corrections (beam angle and DPP) a decrease to 2% LDD, although attractive, is not fully justified for the moment, especially with complex plans that have a higher number of lateral beams.

It would also be interesting to investigate errors incorporated directly into clinical plans. However, introducing errors such as modified angles or beam sizes, which have been simulated for other techniques [9,10] is currently not feasible due to the CyberKnife system architecture. We therefore think that the use of our test scenarios is a valuable compromise for a first validation of the method sensitivity.

Lastly, caution is advised with the 1000SRS when verifying treatment plans that have very small target volumes and use the smallest collimators (5 mm and 7.5 mm). Due to volume effects, the resolution of the 1000SRS and the Gamma-Index analysis method errors in small field verification could be large and need to be evaluated in more detail. Other methods such as DVH- or spatial pixel-dose analysis [19,21,22] and the possibility to analyze passing rate as a function of gamma tolerance or gamma distance may be more meaningful than Gamma-Index analysis alone. Nevertheless, the presented results highlight that 1000SRS can be used for reliable CyberKnife DQA, and it is a valid alternative to film, permitting to overcome film dosimetry limitations in terms of long waiting times and absolute dose uncertainties. Automatic array-to-plan registration and a beam-by-beam SDD and angle correction are under investigation and may expedite the DQA analysis, alleviating QA burden while increasing the number of clinical plans to be verified. A discussion on the necessary frequency for the laborious CyberKnife DQA is beyond the scope of this paper, but requires further investigation [23].

5. Conclusion

We demonstrated that a high-resolution liquid-filled ion-chamber array is suitable for robotic radiosurgery DQA and that despite non-corrected beam angle response differences and variable SDD the results were comparable to those obtained by film dosimetry. We also demonstrated that small system errors can be detected with tight Gamma-Index criteria and we provided various test scenarios to validate the detector sensitivity for robotic radiosurgery delivery quality assurance. Our proposed tolerance levels were validated on a considerable number of clinical plans obtained at five different centers. Further improvement may come from beam specific angle and SDD corrections.

Conflict of interest

None.

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