Physics and Imaging in Radiation Oncology 23 (2022) 60–65

Contents lists available at ScienceDirect

Physics and Imaging in Radiation Oncology

journal homepage: www.sciencedirect.com/journal/physics-and-imaging-in-radiation-oncology

Original Research Article

Dosimetric effects of embolization material artefacts in arteriovenous malformations stereotactic radiosurgery on treatment planning calculation

Abousaleh Elawadi [a,b], Mukhtar Alshanqity [a,*], Hussain AlHussain [a], Reham Mohamed [a,c], Yasser Orz [a], Sultan Alqahtani [a], Sayel Melheim [a]

[a] King Fahad Medical City, Riyad, Saudi Arabia
[b] Faculty of Medicine, Mansoura University, Egypt
[c] National Cancer Institute, Cairo University, Egypt

ARTICLE INFO

Keywords:
Embolic materials
Stereotactic radiosurgery
Arteriovenous malformations

ABSTRACT

Background and Purpose: Stereotactic Radiosurgery (SRS) is a specialized radiotherapy treatment technique for Arteriovenous Malformations (AVM) in which Computed Tomography (CT) images are used for dose calculations. The purpose of this study was to investigate CT image distortions caused by embolic agents and quantify the influence of these distortions on dose calculations.

Methods: Eight AVM patients administered embolic agents prior to SRS were included. Original plans were compared to new recalculated plans using two sets of images. The first set was created by masking the embolic material and artefacts, the second was the diagnostic CT images. In addition, treatment plans were created for an anthropomorphic phantom with water inserts, then with known volumes of embolic materials to study the dosimetric effect of each material.

Results: Relative to patients' original plans, maximum Monitor Unit (MU) difference was −4.4% with whole brain masking, −1.3% with artefact masking, −4.1% with embolic masking, and −4.5% with artefact-free diagnostic images. Calculated dose differences were within ± 3.5% for all plans. In phantom, Gamma pass rate was 96% for both embolic agents with conformal fields and 99.9% with dynamic arcs. Dose and MU differences in phantom plans were negligible.

Conclusion: Relative dose differences between the original plans and the corrected ones were not clinically remarkable. We recommend evaluating the effect of embolic materials on individual patients' plans. The whole brain corrected planning CT images or diagnostic CT images could be utilized to calculate the magnitude of dose reduction caused by embolic materials and correct it if necessary.

1. Introduction:

Arteriovenous Malformations (AVM) are congenital lesions of abnormal blood vessels [1–4]. It is estimated that one person in 100,000 will develop AVM annually [5]. For younger people, AVM's are the main cause of non-traumatic intracerebral hemorrhage [6]. In addition to surgery and embolization, AVM management options include Stereotactic Radiosurgery (SRS) [4,7,8], which is a specialized technique that delivers highly focused and conformal radiation dose to a small planning target volume (PTV) in a single fraction. Embolization is an invasive procedure that involves the injection of embolic materials into the AVM to obstruct blood flow from feeding arteries [9].

Computed Tomography (CT) imaging is the most suitable modality for radiotherapy treatment planning systems (TPS), due to its geometrical accuracy and electron density data. CT images however may suffer some imaging artefacts due to the presence of high density materials such as dental fillings, prosthetic implants, and contrast agents. These imaging artefacts could alter the measurable CT numbers.

Some AVM patients undergo embolization procedures prior to SRS treatments [8]. Embolic materials usually remain in the AVM for prolonged periods of time. Consequently, radiotherapy planning CT images for these patients often include artefacts arising from residual embolic materials. The artefacts can be severe and may result in considerable changes in the CT numbers that masks anatomy and cause misperception, see Fig. 1, which in turn may reduce the dose calculations accuracy.

Many published studies have investigated the effect of contrast

* Corresponding author.
E-mail address: malshanqity@kfmc.med.sa (M. Alshanqity).

https://doi.org/10.1016/j.phro.2022.06.014
Received 17 January 2022; Received in revised form 13 June 2022; Accepted 28 June 2022
Available online 2 July 2022
2405-6316/© 2022 The Authors. Published by Elsevier B.V. on behalf of European Society of Radiotherapy & Oncology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

agents on radiotherapy dose calculations [10–16], however, fewer studies investigated the influence of embolic materials. The reviewed published articles on the subject can be divided into two groups, first group acknowledged the effect and recommended dosimetric corrections [17–20]. The second group reported no significant dosimetric changes [21–24]. However, these reports were generally based on simplified treatment plan simulations with rigid phantoms, and mostly used a single beam with regular-shaped targets, which are not realistic clinical representations. As an example of the second group, Roberts et al [23] measured the attenuation of large embolic material samples on a solid phantom using a parallel plate ionization chamber. Although the study reported that the radiation beam was attenuated by 1.0% for 6 MV photons, the authors recommend further study to evaluate the effect on dose calculations. In a study on the effect of a similar embolic agent [24], the authors measured the attenuation factors for the embolic material in its liquid form and as a solid after it was mixed with blood. Then they overwrote the CT numbers in a group of 16 patients that was previously treated. They concluded that a dose correction is necessary to reduce inaccuracies in treatment delivery. On the contrary, another similar study [18] has concluded that the embolic material did not reduce the radiation dose delivered by 4-Arcs treatment plan to a plastic water phantom. A similar conclusion was also drawn in another study that investigated the dosimetric properties of different embolic materials in two scenarios [19]. First in the presence of Tantalum powder, which is a radiopaque agent used in some embolic materials, and second when Tantalum powder was not used. The results from this study suggested that the dosimetric properties of the embolization agents were similar to those of water for a 6 MV beam. Other investigators [21] concluded a dose reduction from 10% to 14.9% when different concentrations of the embolization materials were used for a solid water phantom. Similarly, another study [22] investigated the effect of the embolization material on the accuracy of dose calculation in clinical setups and concluded that the pencil beam (PB) dose calculation algorithm overestimates the calculated dose.

The primary aim of this study was to quantify the dosimetric effects of the embolic materials on the AVM treatment planning dose calculations in clinically relevant scenarios. Furthermore, possible reduction methods to these effects were investigated.

2. Materials and Methods:

This study was approved by our institutional review board, (IRB 18–688). The AVM treatment program in our institution is based on linear accelerators (Linacs). The Linacs used were beam-matched dual energy HDX machines (Varian Medical System, Palo Alto, USA), equipped with high definition Multi-Leaf Collimators. Treatment plans were developed using iPlan TPS version 4.5.5 with a PB dose calculation algorithm (BrainLab AG, Feldkirchen, Germany). CT images were acquired using a large-bore radiotherapy CT simulator (Somatom, Siemens, Germany) according to the departmental protocol for Brain SRS treatment.

Two embolic agents were evaluated in this study, Onyx^{TM} (Micro Therapeutics Inc., Irvine, CA, USA) and Phil^{TM} (Microvention Europe, Saint-Germain-en-Laye, France). Onyx is a non-adhesive liquid embolic agent comprised of ethylene vinyl alcohol copolymer dissolved in dimethyl sulfoxide and suspended micronized Tantalum powder to provide contrast. Phil is also a non-adhesive liquid embolic agent comprised of co-polymer dissolved in dimethyl sulfoxide with an iodine component to provide radio-opaqueness.

Patients selection criteria included AVM patients who underwent SRS treatment following embolization and had pre-embolization diagnostic CT images that satisfy the three-dimensional registration accuracy

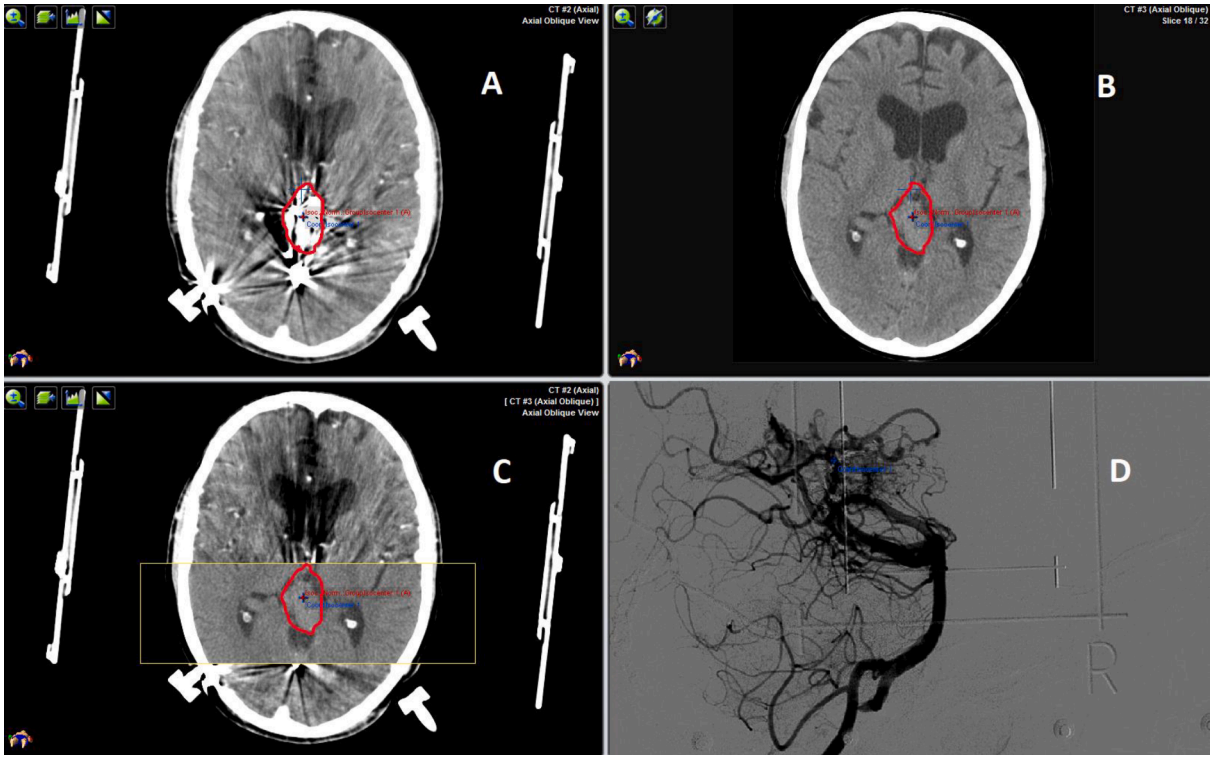

Fig. 1. Embolic materials cause significant artefacts that may interfere with dose calculations and obscure the anatomy. The image is for an AVM patient (case1) several months after embolization. The streaks in subfigures A and C are a result of photon scatter and beam hardening due to the presence of high density embolic material, both bright and dark streaks are visible in this image. AVM in demarcated in red contours: A) CT planning image showing the embolic material and associated artefacts, the SRS frame and posterior fixation screws also shown, B) diagnostic CT image acquired prior to the administration of the embolic material, C) Planning and diagnostic CT image blend, and D) Lateral angiograph image showing the blood vessels and the AVM, the embolic material itself is so small that it cannot be seen. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

criteria of 0.2 mm and 0.1° when rigidly registered to planning CT images. Eight patients met the criteria, one patient was administered Phil, one patient had Phil following Onyx, and Onyx alone was administered to the other six patients. Two treatments were delivered with dynamic arcs and the remaining six were delivered using static conformal beams, Table 1.

2.1. Dosimetric investigation of embolization materials

The study design included two separate methods, the first was based on CT number masking of artefacts using patients' radiotherapy treatment planning CT images. In the second method, artefact-free pre-embolization diagnostic CT images were used for dose calculations. Treatment plans based on both image sets were compared to the original treatment plans in terms of MU and dose calculation. In addition, two different SRS plan templates were calculated in a standard setup using a rigid anthropomorphic phantom with custom inserts filled with known volumes of water and embolic agents. The phantom used was a head Alderson Anthropomorphic phantom (Radiology Support Devices, Long Beach, CA, USA).

2.2. CT numbers masking method

Using the original planning CT images, three structures were created to demarcate the volumes of interest. These were Embolic Material Structure (EMS), Image Artefacts Structure (IAS), and Whole Brain Structure (WBS). The structures were contoured in CT images at variable viewing window levels to accurately define the volumes of interest. Then, the respective CT number values were overridden and assigned to water, i.e. 0 HU. The goal was to replace the extreme density artefacts in CT images with water equivalent density which is a reasonable radiological tissue substitute.

IAS was created by subtracting EMS from WBS to represent the artefact affected volume within the brain. Effects of embolic materials and image artefacts on absolute dose and MU were evaluated by calculating the percentage difference (PD), Equation (1), between the CT-masked plans and the original treatment plans.

$$PD = 100^{*}\frac{(Cv - Dv)}{Dv} \quad (1)$$

Cv is a point dose value in CT–masked plan and Dv is the corresponding value in the original treatment plan that shares the same coordinate. Dose values were compared using PD for a variety of dose metrics, including maximum, mean, and minimum in the AVM target volume.

Table 1
Summary of the 8 patients included in the study with prescribed dose (Gy), AVM volume (cc), Embolic Material Structure (EMS) volume (cc), AVM and EMS overlapping (intersection) volume (cc), and the treatment technique. NI indicates no intersection.

Case	Prescribed Dose (Gy)	AVM Volume (cc)	EMS Volume (cc)	AVM and EMS Intersection Volume (cc)	Treatment Technique
1	15	9.2	22.2	1.3	7 Conformal Fields
2	18	15.5	7.5	4.8	4 Dynamic Arcs
3	20	3.0	2.9	1.0	7 Conformal Fields
4	22	0.9	3.6	0.1	12 Conformal Fields
5	16	10.2	3.2	2.8	9 Dynamic Arc Fields
6	20	3.0	1.5	NI	7 Conformal Fields
7	22	0.1	0.9	0.0	7 Conformal Fields
8	21.8	0.3	4.8	0.1	7 Conformal Fields

2.3. Artefact-Free diagnostic CT images method

Artefact-free diagnostic images acquired prior to embolization were used for dose calculation. Original radiotherapy planning CT images were replaced by these diagnostic CT images. A dedicated calibration curve for each diagnostic CT machine was used for dose calculation relevant to the diagnostic CT image set in use. The diagnostic CT images were rigidly registered to the planning CT images, Fig. 1. Then, MU and dose values were recalculated without optimization or modifications to the plan parameters. Similar to the first method, Equation (1) was used to quantify differences between diagnostic CT-based plans and the original plans. Furthermore, dose differences were assessed using three dimensional (3-D) gamma evaluation with three criteria levels; distance-to-agreement (DTA) of 1.0 mm and dose-difference (DD) of 1.0%, DTA 1.0 mm and DD 2.0%, and DTA 1 mm and DD 3.0%. In addition, 10% threshold was applied to eliminate low dose error over-estimation [25].

2.4. Anthropomorphic phantom dosimetric evaluation

Known volumes of the two embolic materials and water were placed inside an anthropomorphic phantom to evaluate the effect on MU calculation and dose values. The head part of the phantom was used to insert cylindrical plastic tubes containing water, Onyx, or Phil, demonstrated in Fig. 2 and Supplementary Fig. S1. Two tubes of each material were used in tandem. All CT images were acquired with a slice thickness of 1.5 mm using the same departmental radiotherapy SRS CT head protocol. The six tubes had identical dimensions, the first pair contained 1.8 ml mixture made of 1.5 ml Phil material diluted with 0.3 ml of water, the second pair contained 1.8 ml mixture made of 1.5 ml Onyx material diluted with 0.3 ml of water. The third pair contained 1.8 ml of water. Water was added to the embolic agents to make it easier to handle and simulate the effect of blood on the embolic material.

The planning goal was to deliver 20 Gy in a single fraction to a spherical 5.6 cm^3 PTV located in the center of the phantom. Dose differences between the three calculated plans were evaluated using VeriSoft software package version 5.1 (PTW-Freiburg, Germany). Comparisons were based on 3-D gamma analysis with distance-to-agreement (DTA) of 1.0 mm and dose-difference (DD) of 1.0% criteria. In addition, 10% threshold was applied to eliminate low dose error over-estimation [25].

2.5. Statistical analysis

Statistical evaluation of the results was performed using the Statistical Package for Social Sciences (SPSS) version 25 (SPSS Inc., Chicago, IL, USA). Alpha level p-value $\leq$ 0.05 was considered statistically significant, while p-value greater than 0.05 was considered statistically non-significant. Data were evaluated for normality, then the proper statistical test is chosen to determine the significance of the difference between the data sets according to the following steps:

1. Shapiro-Wilk normality test that shows whether a dataset is distributed normally or exhibits a non-normal distributions [26].
2. Mann-Whitney-Wilcoxon test to evaluate the differences between two independent non-normal distributions [27].
3. Student's T-test to evaluate the difference between two independent normal distributions [28].

3. Results

CT numbers Masking Method and Artefact-Free Diagnostic CT Images Method.

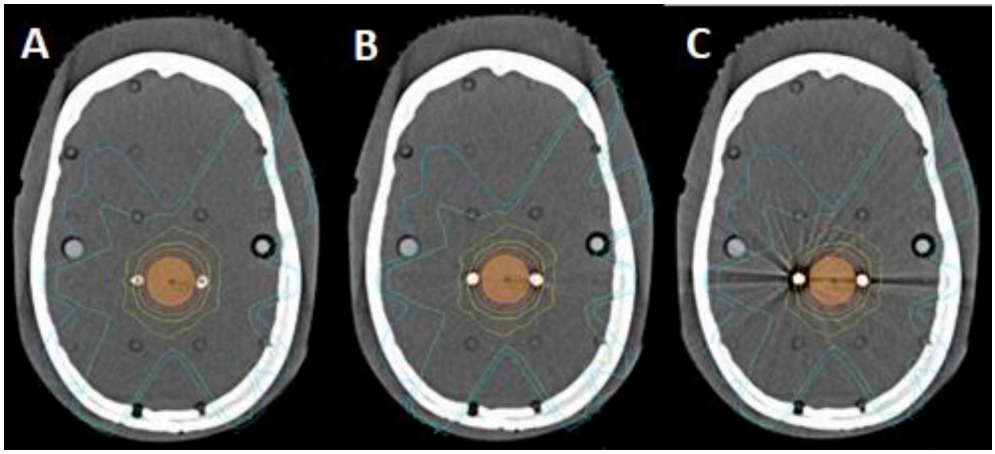

Fig. 2. Axial CT images for the anthropomorphic phantom using Water (A), Phil (B), and Onyx (C) showing the PTV (orange circle) and 10% (Cyan) to 100% (Red) isodose lines for the 20 Gy prescription. No artefacts are seen in image A, while artefacts are clear in the other two, with Onyx resulting in more intense atrefacts. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Calculated MU were found to be normally distributed in all plans. T-test indicated statistically significant differences between original treatment plans and CT number masking based plans while no statistically significant differences were found between WBS masked and diagnostic image based plans ($p = 0.07$).

Differences in the calculated MU values using IAS, EMS, WBS, and diagnostic image based plans relative to the original calculated MU are listed in Table 2. The absolute mean difference was lowest with IAS (0.8%), while the differences were three times higher than the value with the other three correction methods. In addition, calculated MU values were similar in WBS and diagnostic image based plans, the maximum difference in MU between the two is within 1%.

The mean calculated PTV dose values were normally distributed for all plans. T-test indicated a statistically significant difference in calculated mean dose between original plans and WBS plans, $p = 0.04$. On the other hand, no statistically significant differences were found between calculated mean dose using diagnostic images based plans and either original plans, $p = 0.06$, or WBS plans, $p = 0.6$. The differences were noticeably higher between the original plans and both WBS and diagnostic image plans, Table 3, maximum absolute difference 3.5%. When comparing WBS and diagnostic image plans, the maximum absolute difference was 2.1%. With regard to the calculated dose, gamma evaluation revealed that some cases (3 cases out of 8 cases, at 1 mm/3%) did not pass the gamma criteria (95%, Supplementary Table S1).

Table 2
Percentage differences in MU compared to the original plans. (IAS) when the artefacts were masked, (EMS) when the embolic material was masked, (WBS) when the whole brain was masked, and diagnostic image when artefact free diagnostic images were used. Percentage Difference (PD) is calculated using Equation (1) for the total calculated MU values with the four different CT images relative to MU in the original plans.

Case No.	Material	IAS (%)	EMS (%)	WBS (%)	Diagnostic Image (%)
1	Onyx	−0.9	−3.5	−4.3	−4.3
2	Onyx + Phil	−0.9	−1.0	−1.9	−1.5
3	Onyx	−0.8	−3.1	−3.7	−3.6
4	Onyx	−1.3	−1.8	−2.8	−2.5
5	Phil	−0.8	−2.0	−2.8	−1.8
6	Onyx	−0.9	−0.9	−0.9	−0.9
7	Onyx	−0.5	0.0	−0.5	0.6
8	Onyx	−0.2	−4.1	−4.4	−4.5
Maximum		−0.2	0.0	−0.5	0.6
Minimum		−1.3	−4.1	−4.4	−4.5
Mean		−0.8	−2.1	−2.7	−2.3

The 3-D gamma index pass rate for Anthropomorphic Phantom dosimetric investigation was 96% for both water versus Onyx and water versus Phil when conformal fields were used, while it was 99.9% for both embolic agents against water with dynamic arc plans. Dose and MU differences between the plans for the two embolic materials and that with water insert were negligible, Table 4.

4. Discussion

This study investigated the dosimetric effects of SRS planning CT image artefacts induced by two embolic materials. Calculated MU and dose values in the original plans were compared to plans based on corrected CT images and artefact-free diagnostic CT images. In addition, the dosimetric effects of the two embolic materials were investigated in phantom. The results suggested that the dosimetric effects of the two embolic materials were not clinically remarkable.

There were no clinically remarkable differences in the calculated MU values relative to the original treatment plans. Several other factors could contribute to the deviations in dose calculation such as the AVM volume, embolic material composition, and the proximity of the residual embolic material to the AVM target volume in addition to the intersection volume between the AVM target and embolic material as in cases 1 and 8 (see Table 1 and Fig. 1).

When distortions from the artefact and embolic material were corrected using WBS masking volume, relative differences in MU were equivalent to the sum of relative differences in IAS and EMS. In addition, the observed relative differences with WBS were equivalent to those obtained from diagnostic image plans. Which suggest that the embolic material volume was the main contributor to the differences in MU and dose values. This can be demonstrated clearly in case number 6 which has the same relative MU difference (-0.9%) regardless of the correction method due the relatively small physical embolic volume (1.49 cc) and its distal location to a larger AVM (3.05 cc), Supplementary Fig. S2.

In terms of dose difference, Olga et al [22] reported that PB calculations over-estimated dose values by more than 4%. This study indicated that mean dose differences between patient treatment plans and WBS based plans were statistically significant, however these differences were clinically unremarkable. When diagnostic images were used for dose calculations, dose differences were found to be statistical insignificant. Mean dose differences between original treatment plans and WBS corrected plans were marginal. This suggests that both diagnostic images and WBS masked images are good methods to estimate the dosimetric effect of embolic materials.

Although the maximum, minimum, and mean difference values indicated insignificant differences in dose values, gamma evaluation

Table 3
Maximum, minimum, and mean percentage dose differnces between the WBS corrected plans, diagnostic images based plans, and orginal plans for the eight patient plans in the study.

	Percentage Difference in	1	2	3	4	5	6	7	8
WBS vs. Original plan	Maximum Dose	−2.9	−0.3	−2.6	−0.4	−1.9	−0.1	0.0	−1.7
	Mean Dose	−1.9	0.3	−2.0	−0.5	−0.8	0.0	0.1	−1.2
	Minimum Dose	−3.5	−0.2	−2.4	0.1	−1.6	0.1	0.0	−0.9
Diagnostic image plan vs. Original plan	Maximum Dose	−2.8	−0.2	−2.5	−0.2	−1.8	−0.2	0.0	−1.6
	Mean Dose	−1.8	0.3	−2.1	−0.1	−0.8	−0.2	0.1	−1.3
	Minimum Dose	−1.3	−1.1	−2.7	0.3	−1.9	−2.6	0.0	−1.0
WBS vs. Diagnostic image plan	Maximum Dose	−0.1	−0.1	−0.1	−0.1	−0.2	0.1	0.0	−0.1
	Mean Dose	−0.1	−0.1	0.1	−0.4	0.0	0.2	0.0	0.1
	Minimum Dose	−2.2	0.9	0.3	−0.2	0.3	2.7	0.0	0.1

Table 4
Percentage differences in MU and dose values metrics relative to plans with water inserts in the anthropomorphic phantom.

	Onyx (%)	Phil (%)
Relative MU Difference	0.02	0.14
Minimum Dose Difference	0.05	0.05
Maximum Dose Difference	0.54	−0.15
Mean Dose Difference	0.05	−0.05

suggested otherwise. There were clinically significant differences in some cases. Gamma evaluation describes a global three dimensional deferential comparisons for all points in the region of interest not only finite maximum or minimum values [25,29]. A robust planning strategy that includes dosimetric evaluation is important for AVM radiotherapy treatments to achieve obliteration and reduce the probability of recurrent hemorrhage. Thus, even if the differences in absolute dose values seems to be insignificant the clinical implications could be significant if the dose value is close to the minimum dose to achieve obliteration. When the minimum prescribed dose for an AVM is 12 Gy, the obliteration probability based on Karlsson-Lax and Flickinger radiobiological models are 49.0% and 39.3% respectively [22]. If the treatment planning algorithm overestimates the dose by 3.5% similar to result in Table 3, which renders 11.64 Gy, the obliteration probability will be decreased to 47.8% and 36.0% for Karlsson and Flickinger respectively. Thus, we recommend to correct the CT images used for dose calculations whenever the prescribed dose is in the range of 12 Gy to 15 Gy by using either WBS masking method or diagnostic images based planning to minimize the risk of unsuccessful AVM obliteration.

The dosimetric effects of known volumes of Onyx and Phil were evaluated in an anthropomorphic phantom. Three-dimensional gamma evaluation was used with strict criteria of 1 mm DTA and 1% local dose difference. Results indicated that the dosimetric effects of both embolic materials were clinically unremarkable when conformal static fields and dynamic arcs were used. Gamma index pass rates were 96% and 99.9% for water versus Onyx and water versus Phil respectively. This is due to the distribution of incident radiation on multiple beam projections where the dosimetric effect of the embolic material is reduced by primary beam contributions from different angles. Therefore, the presence of radiologically-dense embolic materials seems to mainly attenuate primary beams going through the embolic material. A similar finding was reported by a Monte Carlo study [30] that used the same gamma evaluation criteria to evaluate dose calculations in presence of Onyx relative to water, they reported a 98.2% gamma passing rate which indicates clinically unremarkable difference. Even though the Onyx clinical performance is well documented in the literature, there is no significant dose difference between treatment plans based on Phil and Onyx materials. Phil however has less observed artefacts compared to Onyx due to the use of iodine rather than Tantalum. This could make Phil more suitable for accurate delineation of the AVM and surrounding critical structures which is suggested by a recently published review article [31]. Another advantage of Phil embolization is that it does not require special preparation and can be administered directly to the patient.

This work included a small number of SRS patients that underwent embolization and had diagnostic CT images prior to embolization. In addition, only two patients were administered Phil agent, which is a limiting factor even though the statistical analysis confirms the findings of the investigation. The treatment planning system iPlan is designed to handle a maximum CT number of 3071 HU which might increase the uncertainty in dose calculations with denser materials.

In conclusion, embolic materials induced image artefacts may reduce the accuracy of dose calculations. Planning SRS treatments with multiple fields and arcs could moderate the dosimetric effect of image artefacts. Although the relative dose differences between the original plans and the corrected ones obtained in this work were not clinically remarkable, we recommend to evaluate individual patients' treatment plans and make corrections especially when the prescribed dose is in the range of 12 Gy to 15 Gy to minimize the risk of unsuccessful AVM obliteration.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.phro.2022.06.014.

References

[1] Peschillo S, Caporlingua A, Colonnese C, Guidetti G. Brain AVMs: An Endovascular, Surgical, and Radiosurgical Update. Sci World J 2014;2014:834931.
[2] Rubin BA, Brunswick A, Riina H, Kondziolka D. Advances in radiosurgery for arteriovenous malformations of the brain. Neurosurgery 2014;74(Suppl 1):S50–9.
[3] Simonin M. Cerebral Arteriovenous Malformations (AVMs): Causes, Treatment and Research. MOJ Proteom. Bioinformat. 2015;2.
[4] Jiang Z, Zhang X, Wan X, Wei M, Liu Y, Ding C, et al. Efficacy and Safety of Combined Endovascular Embolization and Stereotactic Radiosurgery for Patients with Intracranial Arteriovenous Malformations: A Systematic Review and Meta-Analysis. Biomed Res Int 2021;2021:6686167.
[5] Brown RD, Wiebers DO, Torner JC, O'Fallon WM. Frequency of intracranial hemorrhage as a presenting symptom and subtype analysis: a population-based study of intracranial vascular malformations in Olmsted County. Minnesota J Neurosurg 1996;85:29.
[6] Karhunen PJ, Penttilä A, Erkinjuntti T. Arteriovenous malformation of the brain: Imaging by postmortem angiography. Forensic Sci Int 1990;48:9–19.
[7] Pierot L, Kadziolka K, Litré F, Rousseaux P. Combined Treatment of Brain AVMs with Use of Onyx Embolization followed by Radiosurgery. Am J Neuroradiol 2013;34:1395–400.
[8] Chen C-J, Ding D, Lee C-C, Kearns KN, Pomeraniec IJ, Cifarelli CP, et al. Stereotactic Radiosurgery With Versus Without Embolization for Brain Arteriovenous Malformations. Neurosurgery 2020;88:313–21.
[9] White AH, Smith FT. Computational modelling of the embolization process for the treatment of arteriovenous malformations (AVMs). Math Comput Model 2013;57:1312–24.

[10] Elawadi AA, AlMohsen S, AlGendy R, Allazkani H, Mohamed RA, AlAssaf H, et al. The Effect of Contrast Agents on Dose Calculations of Volumetric Modulated Arc Radiotherapy Plans for Critical Structures. Appl Sci 2021;11:8355.
[11] Aras S, Aktan M, Koç M. Investigation of the Effects on Dose Distributions of Contrast Agents Used in Stomach Cancer Radiotherapy. J Radiol-Special Topics 2017;10:S45–8.
[12] Burridge NA, Rowbottom CG, Burt PA. Effect of contrast enhanced CT scans on heterogeneity corrected dose computations in the lung. J Appl Clin Med Phys 2006; 7:1–12.
[13] Ehtiati A, Hejazi P, Bakhshandeh M, Jabbary Arfaee A, Rajab Bolookat E, Jadidi M, et al. The Effect of Contrast-enhanced Computed Tomography (CT) Scans on the Calculated Dose of Radiotherapy in a Thorax Phantom. Int J Cancer Manag 2021; 14:e84158.
[14] Ercan T, Igdem S, Alco G. The effect of bladder contrast on dose calculation in volumetric modulated arc therapy planning in patients treated for postoperative prostate cancer. Jpn J Radiol 2016;34:376–82.
[15] Gleeson I. Dosimetric effects of bladder and rectal contrast agents in prostate radiotherapy. J Radiother Pract 2013;12:344–51.
[16] Izmirli M, Çakır T, Avcu S, Nart M. Impact of contrast agents on dose algorıthms of planning systems. Int J Radiat Res 2016;14:25–30.
[17] Mamalui-Hunter M, Jiang T, Rich KM, Derdeyn CP, Drzymala RE. Effect of liquid embolic agents on Gamma Knife surgery dosimetry for arteriovenous malformations: Clinical article. J Neurosurg 2011;115:364–70.
[18] Bing F, Doucet R, Lacroix F, Bahary JP, Darsaut T, Roy D, et al. Liquid Embolization Material Reduces the Delivered Radiation Dose: Clinical Myth or Reality? Am J Neuroradiol 2012;33:320–2.
[19] Labby ZE, Chaudhary N, Gemmete JJ, Pandey AS, Roberts DA. Dosimetric measurements of an n-butyl cyanoacrylate embolization material for arteriovenous malformations. Med Phys 2015;42:1739–44.
[20] Wang L, Wang L. Dosimetric Effect of Onyx Embolization on Radiation Treatment of Arteriovenous Malformations With Robotic Radiosurgery: A Monte Carlo Simulation Study. Int J Radiat Oncol Biol Phys 2013;87:S736.
[21] Andrade-Souza YM, Ramani M, Beachey DJ, Scora D, Tsao MN, terBrugge K, et al. Liquid embolisation material reduces the delivered radiation dose: a physical experiment. Acta Neurochir 2008;150:161–4.
[22] Galván de la Cruz OO, Lárraga-Gutiérrez JM, Moreno-Jiménez S, García-Garduño OA, Celis MA. Effect of the embolization material in the dose calculation for stereotactic radiosurgery of arteriovenous malformations. Med Dosim 2013;38: 110–4.
[23] Roberts DA, Balter JM, Chaudhary N, Gemmete JJ, Pandey AS. Dosimetric measurements of Onyx embolization material for stereotactic radiosurgery. Med Phys 2012;39:6672–81.
[24] Shtraus N, Schifter D, Corn BW, Maimon S, Alani S, Frolov V, et al. Radiosurgical treatment planning of AVM following embolization with Onyx: possible dosage error in treatment planning can be averted. J Neuro-Oncol 2010;98:271–6.
[25] Miften M, Olch A, Mihailidis D, Moran J, Pawlicki T, Molineu A, et al. Tolerance limits and methodologies for IMRT measurement-based verification QA: Recommendations of AAPM Task Group No. 218. Med Phys 2018; 45: e53-e83.
[26] Shapiro SS, Wilk MB. An Analysis of Variance Test for Normality (Complete Samples). Biometrika 1965;52:591–611.
[27] Mann HB, Whitney DR. On a Test of Whether one of Two Random Variables is Stochastically Larger than the Other. Ann Math Stat 1947;18:50–60.
[28] Kirkwood BR, Sterne JAC. Essential Medical Statistics. 2nd ed: Wiley-Blackwell; 2003.
[29] Low DA. Gamma dose distribution evaluation tool. South Carolina, USA: IOP Publishing; 2010.
[30] Schlesinger DJ, Nordström H, Lundin A, Xu Z, Sheehan JP. Dosimetric effects of Onyx embolization on Gamma Knife arteriovenous malformation dose distributions. J Neurosurg 2016;125:114–22.
[31] Vollherbst DF, Chapot R, Bendszus M, Glue MMA. Onyx, Squid or PHIL? Liquid Embolic Agents for the Embolization of Cerebral Arteriovenous Malformations and Dural Arteriovenous Fistulas. Clin Neuroradiol 2021.