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PAPER

Radiation dose aspects and establishment of diagnostic reference levels for ^{90}Y radioembolisation during angiographic procedure

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Abstract

^{90}Y radioembolisation (RE) is an angiographic procedure used in patients with both primary and secondary hepatic malignancies. Local tumour control can be achieved by short range tumour irradiation by the regional intra-arterial administration of glass or resin microspheres loaded with 90yttrium that accumulate in the tumorous tissue. The aim of this study was to investigate the radiation exposure of RE and to establish a local diagnostic reference level (DRL). In this retrospective study, dose data from 397 procedures in 306 patients (mean age 67.4 ± 10.6 years, 82 female) who underwent RE between 06/2017 and 01/2022 using one of two different angiography systems were analysed. DRL was set as the 75th percentile of the dose distribution. In the overall population, dose area product (DAP) (median (interquartile range, IQR)) was 26 Gy cm^2 (IQR 12–50) with a median fluoroscopy time (FT) of 4.5 min (IQR 2.9–8.0). FT and DAP increased significantly with the number of infusion positions (median, IQR): one position 23 Gy cm^2 (12–46), two positions 33 Gy cm^2 (14–60), three positions 50 Gy cm^2 (24–82) ($p < 0.0001$). Local DRL is 47 Gy cm^2 for RE and 111 Gy cm^2 for RE with additional embolisation. Radiation exposure and FT are significantly higher with increasing number of infusion positions as well as additional embolisation. Our established DRLs for RE may serve as a benchmark for dose optimisation.

1. Introduction

^{90}Y radioembolisation (RE) is a standardised, endovascular, fluoroscopically guided therapy to treat both primary and secondary hepatic malignancies. Multiple guidelines, such as those of the National Comprehensive Cancer Network [1] and the American Association for the Study of Liver Disease [2], consider the use of RE as a treatment option for hepatocellular carcinoma (HCC), intrahepatic cholangiocarcinoma (ICC), and hepatic metastases [3–7].

In RE, glass or resin microspheres loaded with ^{90}Y are injected into a hepatic artery. As vascular anomalies are common in hepatic malignancies, these microspheres cumulate in the tumour and deliver a high local radiation dose. Due to the short range of the β-radiation emitted by ^{90}Y, effective local tumour control can be ensured by radiation-induced necrosis with low systemic toxicity. By choosing an appropriate vessel, whole liver, lobar or segmental treatment can be performed [8, 9].

The number of performed RE procedures has increased significantly over the past decade. The radiation exposure (of patients and medical staff) associated with the radiopharmaceutical during its preparation and administration is well studied and described in the literature [10–12]. However, data describing the radiation exposure of the angiographic procedure itself is scarce [13].

Although the risk of stochastic radiation damage is not clinically relevant in patients with malignant diseases due to their limited lifespan, overall dose optimisation should be sought to reduce radiation exposure for the staff members performing repeated RE [14, 15]. Therefore, the aim of this study was to investigate radiation exposure associated with the angiographic procedure itself and to establish local diagnostic reference levels (DRLs).

2. Material and methods

2.1. Patient cohort

Dose data of patients who underwent RE between 06/2017 and 01/2022 at our department were included in our study. Patients were identified using the radiology information system, and all data that included clinical information and a report of the intervention were considered. Complete information on dose levels was extracted from the dose-monitoring software Radimetrics™ Enterprise Platform (Bayer Healthcare, Leverkusen, Germany). Ethical approval for this retrospective single-centre study was granted by the local ethics committee and the requirement to obtain informed consent was waived (21-10256-BO).

2.2. Angiography systems

RE was either performed using the biplane angiography system Artis Q biplane (Siemens Healthineers, Erlangen, Germany) in monoplane mode, or the monoplane angiography system Artis zee MP (Siemens Healthineers, Erlangen, Germany). All procedures were performed using the vendors' default abdomen imaging protocol. The automatic adjustment of the tube potential of both angiography systems varied between 60 and 85 kV. Both angiography systems use a 0.1 mm Cu filter and an additional filter was set, depending on the beam-limiting device. Pulsed fluoroscopy was always used with pulse rates of 3 and 7 pulses s^{-1}. To ensure a continuous, high-level system performance, regular quality control checks were performed on all systems during maintenance visits and the dose area product (DAP) metre was calibrated to national standards.

2.3. Selective internal radiation therapy procedure

All patients had undergone pretherapeutic angiographic evaluation including local injection of ^{99m}Tc-labeled macroaggregated albumin (MAA), subsequent planar scintigraphy and SPECT(/CT) to exclude relevant extrahepatic shunting.

Standard RE included transfemoral access via a 5-Fr sheath and fluoroscopically guided access to the previous MAA infusion position was directly probed for whole liver, lobar or segmental treatment. The coeliac trunk was accessed with a Sidewinder No. 1 catheter. After a contrast injection series via the coeliac trunk, a microcatheter (standard: Rebar 27 reinforced microcatheter, Medtronic, Irvine, USA) and microwire (standard: Runthrough NS, Terumo, Tokyo, Japan) were inserted coaxially. Contrast injection series were only performed in the coeliac trunk and from the branches to be infused. In some cases additional protective embolisation with permanent or non-permanent embolic agents (e.g. of the cystic artery or inferior phrenic artery) was performed. After evaluation of the flow conditions in the hepatic arteries, it was decided to inject the ^{90}Y microspheres (TheraSphere©, Boston Scientific, Marlborough, Massachusetts). Finally, the catheter system was rinsed with approximately 20 ml saline solution and the catheter position was documented. Then, the catheter system was removed and a pressure dressing was applied.

2.4. Dose assessment

For dose assessment, we retrieved examination data and dose measurements from the Radiation Dose Structured Report stored in the Picture Archiving and Communication System with the help of the dose-monitoring software and from the Digital Imaging and Communications in Medicine header. Radiation exposure for RE was determined in terms of DAP. To achieve dose optimisation in the clinical routine, DRLs (which were set at the 75th percentile of dose distribution) are a globally accepted element for dose monitoring of interventional procedures typically defined in terms of the DAP [16].

2.5. Statistics and data analysis

Statistical analysis was performed using Statistical Package for Social Sciences v. 27.0. (SPSS Inc., New York, USA). Data were initially assessed for normality by applying the D'Agostino-Pearson test. Normally distributed data are provided as mean ± standard deviation (SD), non-normally distributed data as median and interquartile range (IQR). To compare DAP and fluoroscopy time (FT) between RE with and without embolisation the Mann–Whitney U test was used. The Kruskal–Wallis test with Dunn–Bonferroni post hoc test was performed for the comparison of DAP and FT of RE as a function of the number of infusion positions. A p-value of <0.05 was considered statistically significant.

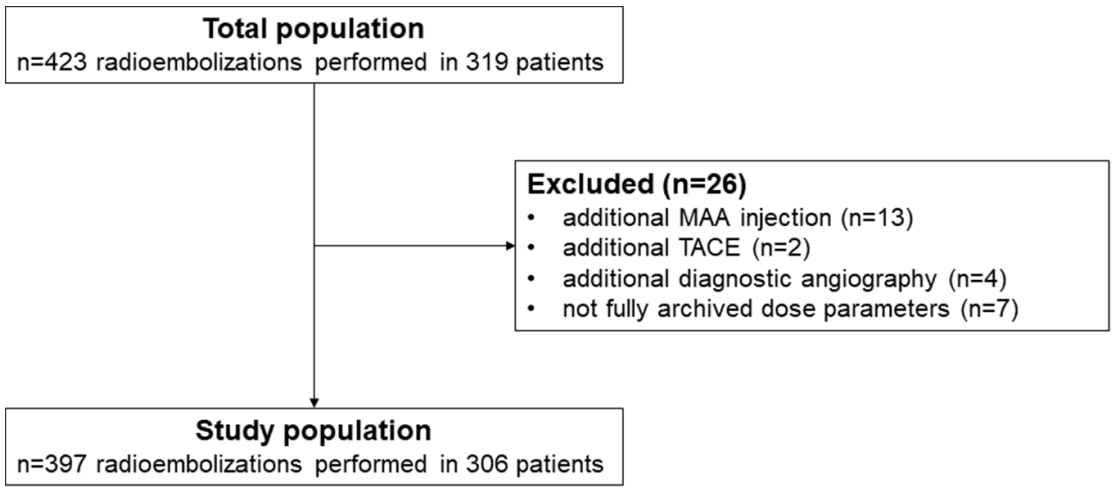

Figure 1. Flowchart of analysed patient cohort with inclusion and exclusion criteria.

2.6. Intraprocedural complications

Three interventions out of 397 were abandoned because of intraprocedural dissection of a vessel (0.3%, 1/397), cardiac complication (0.3%, 1/397), or because of unsuccessful catheter placement in the hepatic branches (0.3%, 1/397). All data were included in the analysis.

3. Results

3.1. Patient cohort

In our retrospective study, 423 REs were performed between 06/2017 and 01/2022, of which a total of 397 REs in 306 patients could be included for evaluation. From a total of 26 excluded procedures, 50% (13/26) were excluded due to additional MAA injection into the contralateral liver lobe. In a smaller proportion of 27% (7/26), dose parameters were not fully archived. Two of the 26 REs were excluded because of additional transarterial chemoembolisation (TACE) and four interventions were excluded because of additional angiographic diagnostic imaging. The inclusion and exclusion criteria are defined in the flowchart (figure 1).

Mean age at first RE was 67.4 ± 10.6 years (range 25–89 years) and 26.8% (82/306) of patients were female. 87 out of 306 (28.4%) patients underwent more than one RE. The largest proportion of the cohort were patients with HCC (in 84.6% (259/306)). In the remaining cases ICC was treated in 5.2% (16/306), hepatic metastases of colorectal cancer in 4.9% (15/306), neuroendocrine neoplasms in 3.6% (11/306), pancreatic carcinoma in 0.7% (2/306), renal cell carcinoma in 0.7% (2/306), and malignant melanoma in 0.3% (1/306). Of all REs, 97% (385/397) were performed on the Artis zee MP angiography system and 3% (12/397) on the Artis Q biplane angiography system.

3.2. Radiation exposure

In the overall population, median radiation exposure of RE in terms of DAP was 26 Gy cm^2 (IQR 12–50 Gy cm^2) (table 1). In REs with embolisation, the median DAP (55 Gy cm^2, IQR 33–111 Gy cm^2, 26/397 REs) was significantly higher by a factor of 2.3 than in interventions without embolisation (24 Gy cm^2, IQR 12–47 Gy cm^2, 371/397 REs) (figure 2). A significant increase in radiation exposure of RE was shown depending on the number of infusion positions ($p < 0.0001$) (median, IQR): one position 23 Gy cm^2 (12–46 Gy cm^2, 301/397 REs), two positions 33 Gy cm^2 (14–60 Gy cm^2, 82/397 REs), three positions 50 Gy cm^2 (24–82 Gy cm^2, 14/397 REs) (figure 3). Thus, median DAP was increased by approximately 42% for two positions and by approximately 116% for three positions compared with RE with only one infusion position. Local DRL is 47 Gy cm^2 for RE and 111 Gy cm^2 for RE with additional embolisation.

3.3. Fluoroscopy time (FT)

The median FT of RE was 4.50 min (IQR 2.90–8.00 min). Spearman's correlation showed a moderate positive correlation between DAP and FT for RE ($r = 0.566$). Embolisation significantly prolonged the median FT of RE from 4.30 to 14.45 min by a factor of 3.36 ($p < 0.0001$). Likewise, FT was significantly prolonged if more than one infusion position was necessary: with two infusion positions, FT was 86% longer (median 6.90 min, IQR 4.70–11.60 min) and with three infusion positions, FT was 267% longer (median

Table 1. Radiation exposure in terms of dose area product (DAP) and fluoroscopy time (FT) of ^{90}Y radioembolization (RE).

		DAP (Gy cm^2)			FT (min)	
RE type	*n*	25th percentile	Median	75th percentile	Median	IQR
Total	397	12	26	50	4.50	2.90–8.00
With embolization	26	33	55	111	14.45	8.20–20.70
Without embolization	371	12	24	47	4.30	2.80–7.30
One position	301	12	23	46	3.70	2.50–6.50
Two positions	82	14	33	60	6.90	4.70–11.60
Three positions	14	24	50	82	9.90	6.20–15.48

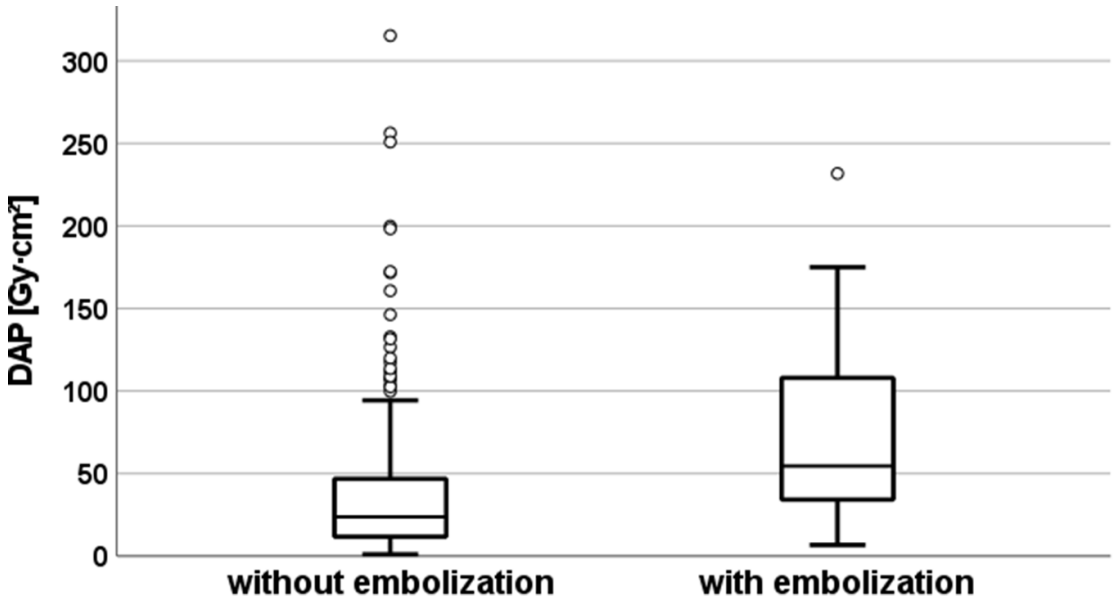

Figure 2. DAP of ^{90}Y RE with and without embolization. Points show outliers outside the Tukey whiskers. Three outliers for the group without embolization and one outlier for the group with embolization, each above 340 Gy cm^2, are not depicted in the graph.

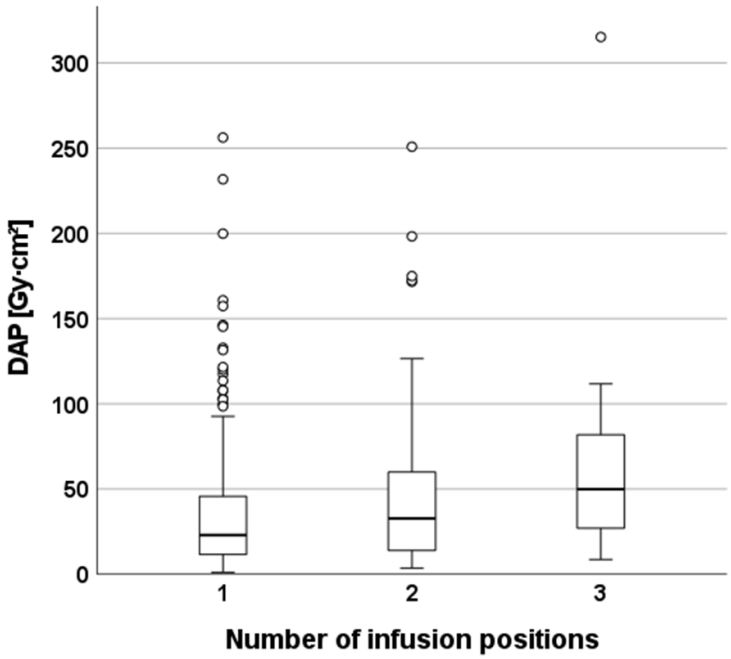

Figure 3. DAP of ^{90}Y RE as a function of the number of infusion positions. Points show outliers outside the Tukey whiskers. For one and two infusion positions two outliers, each above 340 Gy cm^2, are not depicted in the graph.

9.90 min, IQR 6.20–15.48 min) compared with one infusion position (median 3.70 min, IQR 2.50–6.50 min) ($p < 0.0001$) (table 1).

4. Discussion

This retrospective, single-centre study provides detailed dosimetry data for RE as a radiological interventional procedure. In particular, the dedicated consideration of both the number of infusion positions and additional embolisation has, to our knowledge, not been performed until now. The established DRLs in this study could serve as a benchmark for national radiation protection authorities to implement DRLs for RE, as proposed for other interventions such as TACE [16]. Here, further standardisation might lead to a reduction of radiation exposure for patients and interventional radiologists alike.

RE is considered a valuable treatment option for patients with both primary and secondary hepatic malignancies [3–7]. Over the last decade, RE as a fluoroscopically guided radiologic therapy has been introduced into the latest guidelines and used more frequently worldwide [17, 18]. Here, dose optimisation might not only be beneficial for the patient but also for the interventional radiologist and his team in the angiography suite. A helpful benchmark for dose monitoring are DRLs, which indicate typical ionising radiation exposure values in a country, region or an institute [19, 20]. The role of DRLs in interventional radiology has increased in recent years, and the guidelines for radiation protection have been updated to include interventional procedures that are regularly used in clinical routine for quality control and benchmarking between institutions [15, 20, 21]. The goal is to raise awareness of dose and, in the long term, to optimise the modification of equipment, techniques and imaging parameters. However, to our knowledge, detailed data on radiation exposure of RE attributed to the angiographic procedure remain scarce and DRLs are not established internationally, in Europe or nationally. Therefore, it may be a first step to the introduction of novel DRLs in the field of interventional radiology, as proposed by the European Directive 2013/59/Euratom [22].

With regard to liver interventions, some European countries have already established national DRLs for TACE, but not for RE [23]. The German DRL for TACE is 230 Gy cm^2 [16], which is the only established value for angiographic liver interventions and far above our local DRL for RE. Data on x-ray radiation exposure for RE remain scarce and published studies suffer from small patient cohorts. The local DRL and median FT for RE in our study (47 Gy cm^2; 4.5 min) are substantially lower compared to the reported data by D'Alessio *et al* ($n = 12$, mean DAP: 166 Gy cm^2, FT: 16 min) [13]. However, the data of D'Alessio *et al* are outdated, as technical equipment has improved in the meantime and the application of this previously novel method is now much more established.

Because of the high individual variability of procedures within the same type of procedure, the use of DRLs in interventional radiology is challenging. In general, it is recommended to collect radiation data of more than 50 procedures within the same type of procedure to determine a DRL for a single centre [24]. As previous studies have shown, radiation exposure for interventional procedures is much more affected by the complexity of the procedure than by the size and weight of the patient [25]. Therefore, DRLs for interventional procedures should ideally be set according to the type and level of complexity of the procedure. Our results confirm this thesis for RE. In interventions with multiple infusion positions, the catheter positions were changed during the procedure. Consequently, additional radiation exposure and FT was necessary. Hence, radiation exposure and FT for RE are significantly increased in our study for interventions with multiple infusion positions. A second infusion position resulted approximately in a 42% increase in radiation exposure, whereas a third infusion position more than doubled the radiation exposure.

In RE procedures, the patient receives an additional dose from bremsstrahlung during the therapeutic phase, as well as an additional dose in the diagnostic/pre-therapeutic phase due to MAA injection and fluoroscopy study [26]. In this paper, we focused the investigation on radiation exposure of the therapeutic angiographic procedure itself. Consequently, DRLs for diagnostic/pre-therapeutic MAA injection should be defined separately.

The limitations of our study are its retrospective and single-centre study design. Moreover, the obtained dose levels could differ from those obtained at other sites and from other angiography devices. A comparison between the two angiographic systems in our study is not meaningful because of the very small number of examinations on one of the devices. Consequently, the collection of dose data from different centres and angiography devices might be a further step in order to establish a national DRL. However, this preliminary data might serve as an important guide to improve radiation exposure during RE.

5. Conclusion

Radiation exposure and FT for RE are significantly increased for interventions with embolisation, and for interventions with multiple infusion positions. Our established DRLs for RE may serve as a benchmark for dose optimisation.

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Conflict of interests

Benedikt M Schaarschmidt has received a research grant from PharmaCept. J Manuel Weber reports personal fees from Boston Scientific, Terumo, Eli Lilly, and Advanced Accelerator Applications, outside of the submitted work. Jens Theysohn reports personal fees from Boston Scientific, outside the submitted work. All other authors have nothing to disclose.

Ethical statement

All procedures were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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