

## Scientific Article

# Magnetic Resonance Imaging Guided Radiation Therapy for Splenomegaly: Clinical Experiences and Technical Tips



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**Purpose:** Splenomegaly is a common manifestation in chronic lymphoid and myeloid malignancies. Although splenectomy is the preferred treatment for symptomatic splenomegaly, it carries significant risks. Radiation therapy (RT) has traditionally been considered a palliative option. This study explores the use of magnetic resonance guided radiation therapy (MRgRT) for splenic irradiation (SI) in patients with myelofibrosis (MFI) and myelodysplastic/myeloproliferative neoplasms (MDS/MPN).

**Methods:** This single-center retrospective analysis includes patients with MFI and MDS/MPN who underwent MRgRT SI between 2018 and 2022. Ten 1 Gy fractions were delivered to the planning target volume (spleen + 3/5mm margin). An adaptive online/offline strategy has been used to reduce the dose to healthy organs. Dosimetric data and clinical outcomes, including pain relief, gastrointestinal symptoms, and hematological values, were assessed.

**Results:** Twelve patients completed SI without interruption, with supportive transfusions as needed for cytopenias. Pain and gastrointestinal symptom relief was observed in most cases. The mean percentage reduction in spleen volume was 53.61%, with an average craniocaudal extension reduction of 77.78%. Twenty-nine (24.2%) of 120 fractions were online adapted, and 14 (11.7%) were replanned offline. Nonhematological toxicities were not reported. At a median follow-up of 12.9 months, 6 patients died, whereas 9 patients underwent hematopoietic cell transplantation, with 6 of them surviving.

**Conclusion:** This study demonstrates MRgRT SI feasibility in MFI and MDS/MPN patients, offering symptom relief and significant spleen volume reduction. Real-time setup verification and adaptive planning allowed for tailored treatment with reduced margins, minimizing healthy tissue exposure. Larger prospective studies with longer follow-ups are needed to further validate its efficacy and safety.

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Research all data generated and analyzed during this study are included in this published article and will be shared on request to the corresponding author.

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## Introduction

Symptomatic splenomegaly is a condition frequently found in many chronic lymphoid and myeloid

malignancies. One of the chronic myeloproliferative neoplasms (CMPN) often associated with splenomegaly is myelofibrosis (MFI), a rare disease occurring more often in the elderly population. This condition, which may develop as primary (pMFI) or secondary MFI (sMFI), as an evolution of other CMPNs such as polycythemia vera and essential thrombocythemia, is characterized by bone marrow fibrosis, extramedullary hematopoiesis, and cytopenias.<sup>1,2</sup>

Ineffective hemopoiesis and reactive bone marrow fibrosis led to the activation of extramedullary hemopoiesis, mainly originating from the spleen. This process is at the basis of splenomegaly, which sometimes leads to increased cytopenias due to the sequestration and progressive destruction of blood cells.<sup>3</sup> Extremely rarely, splenomegaly is also seen in myelodysplastic syndromes (MDS), characterized by hypercellular bone marrow and peripheral cytopenia due to intramedullary apoptosis of dysplastic clonal cells.<sup>4</sup> In this setting, the pathogenesis of splenomegaly is not entirely understood, but the underlying mechanism is most likely a consequence of the MDS pathogenetic processes described above.<sup>5,6</sup> Specifically, this nosologic entity is better known as myelodysplastic/myeloproliferative neoplasms (MDS/MPN).<sup>7</sup>

Symptoms of splenomegaly are related to the gradual growth of the spleen and include pain, both due to congestion in the abdominal cavity and the onset of splenic infarcts, premature satiety, challenged ingestion, gastric compression, asthenia, and cachexia.<sup>2</sup> Splenectomy is the treatment of choice in symptomatic splenomegaly unresponsive to therapy, although it is associated with high morbidity and mortality rates due to the high risk of bleeding, infection, and thrombosis.<sup>2</sup>

Historically, radiation therapy (RT) has always been reserved in a palliative or salvage setting, in patients unfit for surgery, due to poor performance status or advanced age, or unresponsive to medical therapies.<sup>8</sup> Given the paucity of data in the literature, several studies reported benefits in terms of pain relief, symptom, and cytopenia improvement, as well as a bridge to allogeneic hematopoietic cell transplantation (HCT), which is the only definitive treatment option for these patients.<sup>8-10</sup> Low doses of RT are effectively prescribed for the treatment of splenomegaly. Indeed, the responses in spleen size reduction, pain, and blood count benefit are very fast, without significant toxicity.

The underlying molecular mechanisms are not fully well defined but involve, first, direct radiation-induced cell death, which leads to a reduction of neoplastic cells within the spleen, and second, indirect mechanisms involving non-neoplastic lymphocytes and cytokines stimulating cell-mediated cell death processes.<sup>11,12</sup> This leads to a reduction in spleen volume of more than 50%, and although the RT doses used are low, ranging from a total dose of 0.15 to 30.5 Gy and a dose per fraction of 0.1 to 2.5 Gy, grade 3 and 4 acute hematological toxicities

and mild G1-G2 gastrointestinal toxicities (eg, nausea) according to Radiation Therapy Oncology Group criteria<sup>13</sup> have been reported.<sup>8,9,14</sup>

The most frequently used fractionation is 10 Gy in 10 fractions, as reported in a recent literature review by Zaorsky et al<sup>8</sup> In this context, the most frequently reported RT-related acute toxicities are hematological (94%). Of these, G3-G4 toxicities were found in 82.5% of all toxicities, versus mild G1-G2 gastrointestinal toxicities found in 4.65% of cases. Consequently, this requires the application of customized RT solutions, such as the adoption of treatment margins that consider intrafraction motion, daily online setup verification, but above all, strategies that take into account these rapid and consistent volumetric changes, day after day, in order to avoid irradiation of healthy organs.

Magnetic resonance-guided RT (MRgRT), thanks to better soft tissue imaging, continuous intrafraction target visualization, and most importantly the availability of on-table adaptive replanning, could be very suitable in this framework.<sup>15</sup> These features can be advantageous in both tumor control and treatment management, with good patient tolerability, even in the elderly.<sup>16</sup> The aim of the current study was to describe the clinical characteristics, tolerability profile of the technique, treatment-related toxicity, and outcomes of a single-center case series of patients suffering from splenomegaly caused by both MDS/MPN and CMPN.

## Material and Methods

MDS/MPN and CMPN patients treated at our institution between May 2018 and July 2022 on a low-T MRgRT unit (MRIdian Linac, ViewRay Inc) were included in our retrospective study. The hematology team diagnosed MDS/MPN and CMPN by analyzing blood tests and conducting a bone marrow biopsy. The diagnosis of splenomegaly was made by abdominal ultrasound and/or abdominal magnetic resonance imaging (MRI), whereas the nonindication for surgery was assessed on a case-by-case basis by a specialized surgical team. The indication for splenic irradiation (SI) by MRgRT was given by a radiation oncologist experienced in hematological malignancies, after a thorough clinical examination.

After confirming that there were no contraindications for undergoing the MRI and the proposed procedure, the patient underwent a treatment simulation using the MRIdian system. During the simulation session, MRI images were obtained using the True Fast Imaging with Steady State Precession sequence, alongside a cine-MR on a sagittal plane. The cine-MR enabled the evaluation of target movement to determine whether the patient should be treated with Free Breathing (FB) or Breath-Hold Inspiration (BHI) gating. This phase is used to set the treatment delivery parameters, including setting the region of

interest percentage (ROI%) and relative boundary values to customize the target gating method. The boundary sets the upper limit for the allowable movement of the target volume during treatment, whereas the ROI% represents the maximum percentage of the target structure that is allowed to extend beyond the boundary. The system will automatically stop treatment delivery if the target exceeds the boundary by an amount greater than the predefined ROI%.

Following this, a computed tomography (CT) standard simulation on a helical CT scanner (GE HiSpeed DX/i Spiral) was performed using the same immobilization and positioning devices used during the MRI simulation. CT images were deformably registered to the acquired MR images to generate the electron density map for planning purposes.

In the contouring phase, using the planning MRI scan as primary imaging, adjacent organs at risk (spinal canal, liver, bowel, heart, lung, kidney, and stomach) were delineated; the gross tumor volume (GTV) was the spleen and equal to clinical target volume, and the planning target volume (PTV) was generated according to institutional guidelines with an isotropic expansion of the GTV that goes from 3 mm, for BHI treatment, to 5 mm for FB treatments, taking into account the gating data obtained during the simulation and based on clinical judgment.

The prescribed dose for PTV was 10 Gy in 10 consecutive treatment fractions. The most commonly used fractionation in clinical practice.<sup>8</sup>

Planning was conducted using the dedicated MRIdian treatment-planning system (ViewRay Inc). Intensity-modulated RT plans were created using a step-and-shoot technique. The dose calculation takes into account the impact of the 0.35 T magnetic field.

It should be considered that the Multileaf collimator of the MRIdian Linac system can generate fixed or step-and-shoot conformal intensity-modulated RT radiation fields from  $0.2 \times 0.4 \text{ cm}^2$  to  $27.4 \times 24.1 \text{ cm}^2$  and that the SI requires large treatment volumes and therefore large radiation fields. To overcome the limited spatial aperture of the Multileaf collimator, it is possible to generate planes with a double isocenter, as shown in a recent study.<sup>17</sup>

The position of the 2 isocenters depends on the extension of the PTV, the first (ISO1) was inserted at one-third of the longitudinal extension of the PTV, and the second (ISO2) at 2/3 of the longitudinal extension of the PTV. Typically, on the isocenters, vertical and lateral shifts from the system isocenter are not inserted in order to have more margins in the patient positioning inside the closed bore of the system for avoiding collisions between the couch and bore. For each of the 2 isocenters, from 20 to 30 beam directions are inserted all around the patient in a VMAT-like configuration,<sup>18</sup> avoiding the directions that will cross the edges of the patient couch.

The treatment plan was optimized according to institutional guidelines, which set a target coverage of  $V95\% > 95\%$  and  $V105\% < 5\%$ . The organs at risk (OAR)

constraints were within tolerable limits due to the low prescribed dose, but an “as low as reasonably achievable” approach was always taken in the optimization, trying to avoid hot spots, especially in areas where there was an overlap in the dose delivered by the 2 isocenters.

Taking into account the volumetric reduction that the spleen underwent in the different cases due to the high intrinsic radiosensitivity, an adaptive online or offline RT approach was chosen, depending on the degree of reduction and the patient’s compliance.

Data on the volume and craniocaudal extent of the splenic ROIs in all RT fractions of all patients were collected retrospectively. Treatment time and target coverage as PTV V95% data were also reported.

After completion of RT, patients were followed up with clinical and laboratory examinations at different intervals depending on the underlying pathology. The patient-reported symptoms were then assessed, on the presence of pain or gastrointestinal complaints caused by splenomegaly. Patients meeting the criteria were referred for allograft transplantation. Acute toxicities were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 5.0.<sup>19</sup>

## Results

### Patient characteristics and outcome

Overall, 12 patients, 5 women and 7 men, were included in our retrospective analysis. Three patients had pMFI, 6 had sMFI, and 3 had MDS/MPN. The median age at the time of diagnosis was 48.5 (28-74) years, and at the time of treatment was 57 (45-74) years. All patients completed SI without interruption, supported by red blood cell or platelet transfusions as needed to treat cytopenias. In particular, 8 patients (66.7%) required transfusion support with a median of 4 units (range: 1-5) of red blood cells, and 7 patients (58.3%) required transfusion support with a median of 2 units (range: 1-3) of platelets. The pretreatment and average hematological values during treatment, taking into account any supportive transfusion therapy carried out, are shown in [Table 1](#). Considering the pre-existing condition of severe cytopenias, it is not easy to distinguish possible hematological toxicity from cytopenias due to hypersplenism. No acute gastrointestinal or dermatological toxicities were reported. During RT, 7 (58.3%) patients received ruxolitinib, 2 (16.7%) received ruxolitinib + hydroxyurea, and 2 (16.7%) received hydroxyurea.

Patient characteristics are shown in [Table 1](#).

Considering the pre-RT clinical situation, 5 (41.7%) patients had reported pain, 10 (83.3%) reported gastrointestinal discomfort. Post-RT, pain had improved in all 5 (100%) cases, whereas gastrointestinal discomfort

**Table 1 Patients clinical characteristic**

Patient	Gender	Age at RT treatment time (y)	Primary disease	ECOG	Pre-RT status				RT status				Post-RT status		
					Hb, g/dL	WBC, $\times 10^9/L$	PLTs, $\times 10^9/L$	Symptoms	Hb, g/dL (average)	WBC, $\times 10^9/L$ (average)	PLTs, $\times 10^9/L$ (average)	Concurrent therapy	Symptoms relief	Post-RT treatments	Follow-up status
1	Female	59	sMFI	0	8.9	7.100	96	Pain	8.72	1.715	86.2	Ruxolitinib, hydroxyurea	Yes	HCT	Deceased
2	Male	59	sMFI	0	9.4	3.750	215	Gastrointestinal complaints	9.7	1.183	171	Ruxolitinib	Stability	Ruxolitinib, HCT	
3	Female	45	pMFI	2	8.9	3.770	40	Gastrointestinal complaints	8.3	4.155	36	Ruxolitinib	Stability	HCT	
4	Female	58	sMFI	0	9	11.100	53	Pain, gastrointestinal complaints	7.9	3.212	38.8	Ruxolitinib, hydroxyurea	Yes	HCT	
5	Male	69	MDS/MPN	0	8.3	2.940	15	Gastrointestinal complaints	8.1	1.500	9		Stability	Hydroxyurea	Deceased
6	Male	61	pMFI	1	11.6	2.910	36	Gastrointestinal complaints	11.2	10.044	61.2	Ruxolitinib	Stability	HCT	
7	Male	56	sMFI	1	8	7.430	567	Gastrointestinal complaints	8	7.430	567	Ruxolitinib	Stability	HCT	Deceased
8	Female	50	pMFI	0	8.4	3.687	415	Pain, gastrointestinal complaints	8.4	4.890	194	Hydroxyurea	Yes		Deceased
9	Male	74	MDS/MPN	1	7.8	3.040	196	Pain	6.8	12.112	101.2	Hydroxyurea	Yes	Hydroxyurea, Ruxolitinib, Cytarabine	Deceased
10	Male	48	sMFI	0	12.9	4.112	70	Gastrointestinal complaints	13.5	28.55	91	Ruxolitinib	Stability	HCT	
11	Male	56	sMFI	1	11	3.640	171	Gastrointestinal complaints, pain	11.9	14.87	178	Ruxolitinib	Yes	HCT	
12	Female	56	MDS/MPN	1	7.5	11.700	130	Gastrointestinal complaints	8	9.6	165	Ruxolitinib	Yes	HCT	Deceased

*Abbreviations:* ECOG = Eastern Cooperative Oncology Group; HCT = allogenic hematopoietic cell transplantation; MDS/MPN = myelodysplastic/myeloproliferative neoplasms; PLTs = platelets; pMFI = primary myelofibrosis; RT = radiation therapy; sMFI = secondary myelofibrosis.

remained stable in 5 (50%) patients and improved in 3 (30%). Patients in whom there was no improvement in their gastrointestinal symptoms were managed clinically with supportive medical therapy.

At a median follow-up of 12.9 (1.35-59.8) months, 6 (50%) patients had died. After RT, 9 (75%) patients underwent HCT. Considering the cohort of transplanted patients, 6 (66.7%) are alive with a median survival of 13.6 (1.3-59.8) months.

### Clinical and dosimetric features

Seven out of 12 patients have been treated in the BHI gating technique, whereas the remaining 5 in the FB phase. As reported in Table 2, half of the patients have been online adapted due to anatomic variation and/or improvement of the dose distribution, although not for all the treatment fractions, according to clinical judgment. On the other hand, patients who have not been online adapted have been offline replanned.

The decision to online adapt the plan is made considering the reduction in spleen volume and the possible presence of OAR within the treatment field. However, if the reduction in spleen volume is still clinically acceptable, offline replanning can always be performed on the daily MRI images, acquired directly inside the MR-Linac, when it is believed to bring a benefit in dose conformation and OARs sparing for future treatment fractions so that in the next treatment fraction, a longer online adaptive session for the patient can be avoided.

Of a total of 120 fractions delivered, 29 (24.2%) were delivered using an online adaptive approach and 14 (11.7%) were replanned offline. Over the 10 treatment fractions, considering both the online adaptation and the offline replanning, on average, each patient underwent 3.6 dose

**Table 2 Patients treatment characteristics**

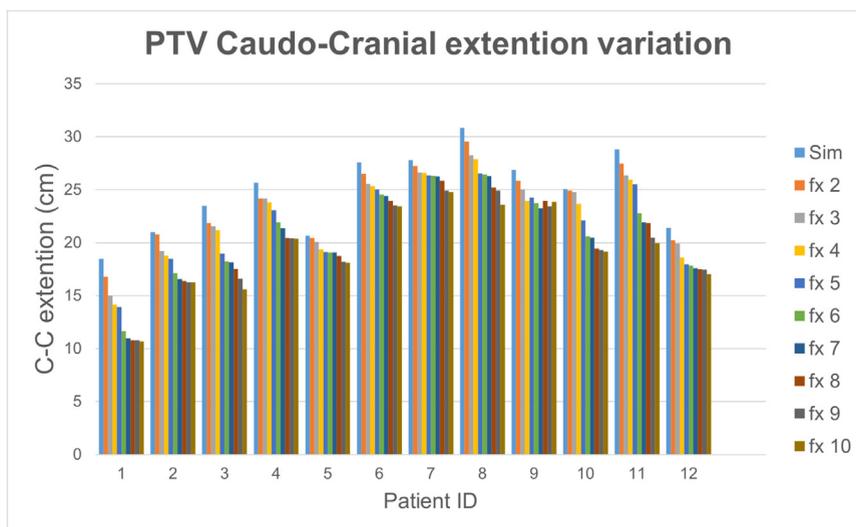
Patient ID	Gating	No. of online adapted fraction	No. of offline replanning
1	BHI	0	3
2	BHI	7	-
3	BHI	4	-
4	BHI	8	-
5	BHI	2	-
6	BHI	4	-
7	BHI	2	-
8	FB	2	3
9	FB	0	2
10	FB	0	1
11	FB	0	2
12	FB	0	3

*Abbreviations: FB = Free Breathing; BHI = Breath-Hold Inspiration.*

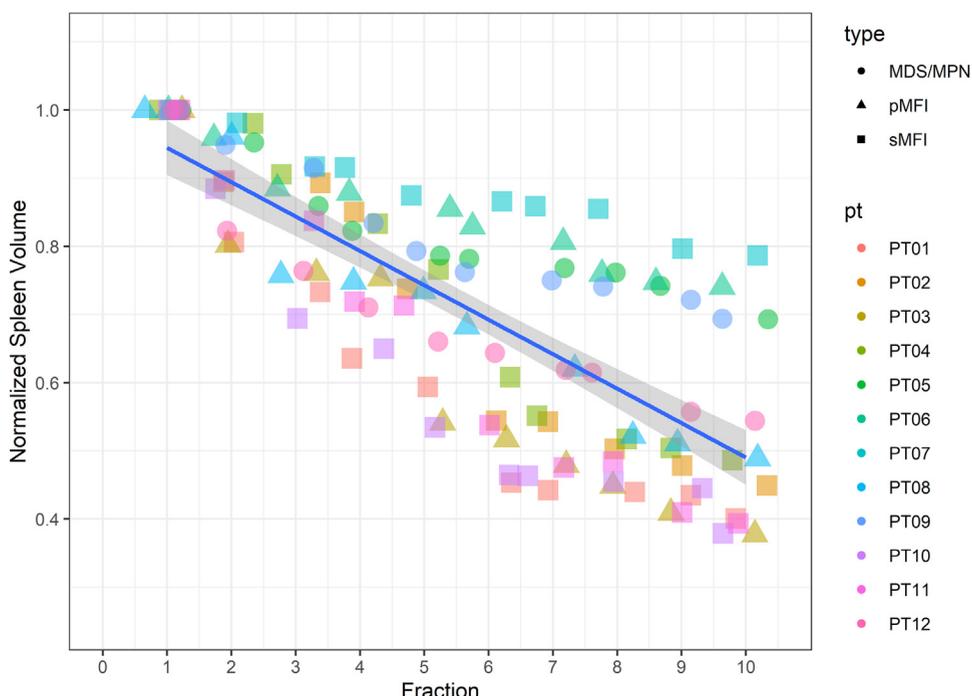
optimizations during the treatment, with a maximum of 8 for patient no. 4 and a minimum of 1 for patient no. 10.

As regards treatment planning, 8/12 patients (66.6%) have been planned with a double isocenter technique, due to the spleen craniocaudal extension. The foreseen PTV reduction has been monitored and measured in terms of the craniocaudal PTV extension throughout the entire treatment. Results of such reductions, for all patients and all treatment fractions (excluding fraction 1 where the PTV CC extension has not been computed since it is the same as the simulation), are reported in Fig. 1.

All patients (100%) had a reduction in spleen size in relation to RT treatment; in Fig. 2, it is possible to see the



**Figure 1** PTV craniocaudal (CC) reduction during RT treatment.



**Figure 2** Normalized spleen volume, measured as the ratio between the spleen volume of the selected treatment fraction and the simulation volume, observed on each treatment fractions for all the patients. Different marks refer to patients with different malignancies. The solid line is a linear fit with a shaded confidence interval.

spleen volume reduction per fraction, the solid line represents a linear fit of the decrease in spleen volume during treatment fractions, whose slope is  $-5.0\% \pm 0.4\%$  per fraction, with an R-squared of 0.6 and a  $P$  value  $<10^{-15}$ . The average percentage change in volume and cranio-caudal extension between the simulation and the last fraction (fraction 10) MRI scan was 53.61% and 77.78%, respectively, as shown in Table 3.

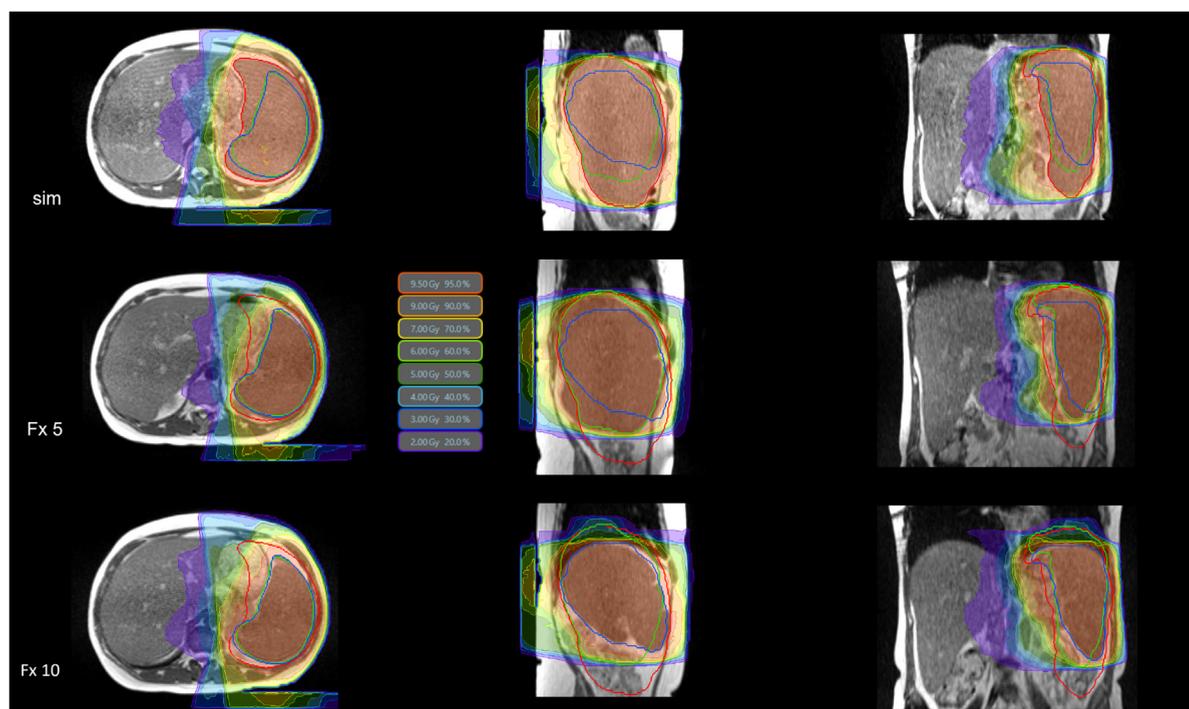
An example of the treatment of a patient using an adaptive approach to take into account the reduction in the size of the spleen is shown in Fig. 3.

As regards treatment time, which is provided by the treatment planning system (TPS) after the dose distribution has been optimized, the mean (min-max) treatment time among the nominal and the adapted plans is 8.6 min (5.4-12.6 min).

**Table 3** Single patient absolute and percentage volume and caudo-cranial extension variation between the simulation and last fraction (fraction 10) MRI scan\*

Patient ID	Volume variation (cc) (%)	Cranio-caudal extension variation (cm) (%)
1	626.3 (40.07)	7.82 (57.71)
2	1981.5 (44.91)	4.74 (77.43)
3	1474.7 (37.75)	7.88 (66.45)
4	1711.4 (48.64)	5.28 (79.43)
5	455.8 (69.30)	2.55 (87.66)
6	912.5 (74.04)	4.13 (85.02)
7	518.1 (78.66)	3.0 (89.20)
8	2090 (48.90)	7.25 (76.49)
9	847.6 (69.38)	3.03 (88.73)
10	2248.9 (37.91)	5.93 (76.35)
11	2486.8 (39.37)	8.84 (69.32)
12	845.4 (54.39)	4.37 (79.59)
Mean	1349.92 (53.61)	5.40 (77.78)

\*Mean value among the entire patient data set is reported in the bottom row.



**Figure 3** Axial, sagittal, and coronal scans of simulation, fraction 5 and fraction 10 of a patient undergoing adaptive MR guided radiation therapy (MRgRT). The structures shown in red, green, and blue and projected at different time points are the splenic segmentations in simulation, fifth and tenth fractions, respectively. The color wash shows the dose distribution of the 3 different adapted treatment plans.

Considering target coverage (PTV V95%) variation of the adapted plan (compared with the nominal plan performed on the simulation MR), the average, maximum, and minimum target coverage improvement among all patients and adapted fractions is 2.3%, 12.8%, and  $-3.5\%$ , respectively. When a plan was adapted, target coverage improved in 60% of the cases; however, a better dose conformation and a reduction of irradiated volumes and dose to OARs were always achieved.

## Discussion

To the best of our knowledge, this is the first case series of patients with both MDS/MPN and MFI who have undergone SI with MRgRT performed with the MR-Linac using both the online and offline adaptive approaches.

Adaptive radiation treatment planning was employed to account for changes in splenic size during treatment. The use of real-time setup verification through MR scans and direct gating of the target during delivery allowed for the implementation of tailored and narrower GTV-PTV treatment margins, ranging from 3 to 5 mm in all directions, based on the chosen gating phase (BHI or FB) on a case-by-case basis, in order to reduce exposure to healthy tissues. Furthermore, the application of adaptive RT protocols enabled adjustments to the treatment plan in response to changes in splenic size throughout the RT

course, thereby preventing unnecessary irradiation of healthy tissues on treatment days.

In addition, dose conformation was improved even in the presence of targets with very voluminous craniocaudal extensions by using the double isocenter irradiation technique to overcome the limited field size of the MR-Linac.<sup>17</sup>

An adaptive CT-based RT study was performed by Sager et al,<sup>9</sup> who retrospectively included 18 patients with splenomegaly, 12 of whom were MFI, and demonstrated the feasibility of a reduction in GTV-PTV margins, to up to 8 mm in craniocaudal and 6 mm in the other directions, based on the study of spleen movement. CT-based adaptive RT holds promise for minimizing exposure to healthy tissue, thus potentially improving outcomes for SI patients by using offline adaptive RT treatment planning to address fluctuations in spleen size during the course of RT. Offline adaptive RT allows for highly personalized treatments to account for tumor shrinkage, although it may have limitations in this context. Indeed, offline adaptive RT may not be able to respond quickly enough to such changes and may induce geometric errors rather than correct them. In addition, it requires the reacquisition of a simulation CT, which in cases such as SI may be necessary more than twice a week, delivering additional doses to the patient and requiring a considerable amount of work between the various figures involved in the workflow (radiation oncologist, medical physicist, radiotherapist, and dosimetrist).<sup>20</sup>

These latter aspects can be implemented by using online adaptive MR guided RT to optimize the process. Indeed, online adaptive RT is used in clinical scenarios where the location and shape of the tumor can vary from day to day, such as lung, prostate, and liver cancers, as well as in situations where proximity to critical structures requires precise targeting (as for the pancreas). Additionally, with an MR-Linac, it is also possible to perform a direct beam gating on cine-MRI during the delivery of the treatment, especially for patients, treated in BHI, whose spleens are affected by big displacement due to respiratory motion. Our study, through continuous monitoring of spleen movement with cine-MRI during the treatment, lowered these margins, with respect to Sager et al,<sup>9</sup> to 3 mm for treatments in BHI and 5 mm for FB, as per internal protocols for all the treatments performed on the MR-Linac in our institution.

We believe that SI could be a clinical scenario where online adaptive RT protocols could potentially be applied, following the sudden volumetric reduction of the spleen while sparing organs from unnecessary irradiation. However, also the use of CBCT-based adaptive systems for SI could be investigated in future studies.

Considering the clinical outcomes, in our case series, we had a 100% reduction in spleen volume. This finding is very interesting when compared with the most recent data in the literature, which range from 62%<sup>3</sup> to 81.8%,<sup>9</sup> with 72% reported in a meta-analysis by Zaorsky et al,<sup>8</sup> although the case series include patients with splenomegaly caused by various medical conditions.

Regarding the extent of reduction, Sager et al<sup>9</sup> and Katano et al<sup>3</sup> observed a reduction in spleen size of 50% and a mean  $\pm$  SD variation rate in spleen volume of  $-19.1 \pm 24.7\%$ , respectively. Furthermore, Ponce et al,<sup>10</sup> in a study of 17 patients, including 14 with MFI, who underwent SI followed by HCT, reported a median craniocaudal reduction in spleen size of 7.3%.

In the present work, the mean percentage change in volume and craniocaudal extension between simulation and final RT fraction was 53.61% and 77.78%, respectively; therefore, our result can be considered very favorable.

In terms of pain relief and associated gastrointestinal symptoms, pain improved in all 5 (100%) patients who reported it before treatment. Gastrointestinal symptoms remained stable in 5 (50%) patients and improved in 3 (30%) patients. Referring to the case histories mentioned above, the palliation rates of pain and other symptoms associated with splenic bulk range from 60% to 90.9%.<sup>3,9</sup>

In addition, the treatment was well tolerated by patients, with none reporting any level of nonhematological toxicity. At the same time, transfusion support, when deemed indicated, allowed treatment to be completed without interruption in all cases.

Although it is clearly not possible to draw conclusions on the benefit of SI as part of HCT conditioning from a

long-term survival outcome perspective due to the retrospective nature of the present study and the small number of patients included, with 75% of patients receiving HCT, this study provides further evidence of the feasibility of this approach in patients with pMFI, sMFI, and MDS/MPN.<sup>10</sup>

We believe that this study can contribute valuable evidence to the current body of literature, which predominantly relies on outdated RT techniques.

MRgRT has emerged as a transformative technology in the field of radiation oncology, offering unique advantages across diverse clinical scenarios, such as stereotactic body RT for lung, liver, and pancreatic tumors, where the ability to track and adapt to tumor motion ensures optimal treatment delivery.<sup>20-25</sup> MRgRT's application also extends to challenging applications, such as the irradiation of peritoneal nodules and cardiac tumors.<sup>26,27</sup>

In the field of hematological malignancies, as demonstrated in our study, MRgRT offers promise in managing splenomegaly, providing rapid symptom relief and substantial spleen volume reduction.

As interesting as this treatment approach is, its retrospective nature, small sample size, and consequently the lack of detailed statistical analysis should be considered when interpreting the results.

Other limitations to be considered are the heterogeneous population included in the study, which may make it difficult to draw specific conclusions on treatment efficacy for each subgroup, and the short follow-up period, especially in patients undergoing HCT, may not give full information on long-term survival outcomes, which are crucial in assessing treatment efficacy.

Furthermore, the absence of a comparison group and comprehensive clinical endpoints warrants a cautious interpretation of the results.

Additional research with larger sample sizes, longer follow-up periods, and more comprehensive outcome measures is needed to better understand the potential benefits and limitations of this treatment approach.

## Conclusions

In this single-center retrospective analysis, we have explored the feasibility of MRgRT for SI in patients with MFI and MDS/MPN. Our findings suggest that MRgRT, with its real-time setup verification, adaptive planning, and reduced treatment margins, offers a promising approach for spleen irradiation, leading to substantial reductions in spleen volume and symptomatic relief.

Moving forward, larger prospective studies with extended follow-up periods and well-defined clinical endpoints are imperative to validate the efficacy and safety of MRgRT in the management of splenomegaly across various hematological conditions. Despite these limitations, our study contributes valuable insights into the potential

of MRgRT as a treatment modality for splenomegaly, offering a glimpse into the evolving landscape of RT techniques in hematological malignancies.

## Disclosures

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