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PERSPECTIVES

Total Marrow and Lymphoid Irradiation (TMLI) - A Paradigm Shift in Radiation-Based Conditioning for Hematopoietic Cell Transplantation

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Abstract

Total Marrow and Lymphoid Irradiation (TMLI) represents a technologically sophisticated evolution of conventional Total Body Irradiation (TBI) in the context of hematopoietic cell transplantation (HCT) conditioning. By harnessing the precision of Intensity Modulated Radiation Therapy (IMRT) delivered via helical tomotherapy or Volumetric Modulated Arc Therapy (VMAT) TMLI selectively irradiates the skeletal bone marrow, major lymph node chains, and spleen while dramatically reducing dose to critical organs at risk. This organ-sparing capacity permits dose escalation beyond the ceiling of conventional TBI (12 Gy), safely achieving doses up to 20 Gy without proportional increases in non-hematopoietic toxicity. Clinical evidence from multiple prospective trials demonstrates that TMLI yields low non-relapse mortality (NRM) rates, favorable overall survival (OS) and progression-free survival (PFS) across a spectrum of disease states including relapsed/refractory acute leukemia, complete remission transplants, haploidentical settings, and elderly patients unsuitable for conventional myeloablative regimens. This review comprehensively examines the radiobiological rationale, technical implementation, target delineation, clinical outcomes, and future directions of TMLI, with the aim of encouraging wider adoption of this transformative technique across Indian transplant centers.

Keywords: Total Marrow and Lymphoid Irradiation, TMLI, Total Body Irradiation, Hematopoietic Cell Transplantation

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1. Introduction

Allogeneic hematopoietic cell transplantation (HCT) remains the only curative option for a significant proportion of patients with high-risk and relapsed/refractory hematologic malignancies. The conditioning regimen employed before graft infusion serves a dual purpose: myeloablation to eradicate residual malignant disease, and immunosuppression to prevent graft rejection. Total Body Irradiation (TBI), typically delivered at 12 Gy in fractionated schedules, has been the cornerstone of conditioning regimens for decades, particularly in acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML). However, conventional TBI carries a well-recognized burden of toxicity. Interstitial pneumonitis, once reported in up to 50% of patients receiving single-fraction TBI, remains a serious complication with fractionated TBI and has been reported at rates as high as 10–85% in published series [1]. Additional toxicities include nephrotoxicity, hypothyroidism, cataract formation, sinusoidal obstruction syndrome (SOS), mucositis, and impaired linear growth in children. Critically, attempts to reduce relapse by simply escalating TBI dose have failed to improve overall survival because increased toxicity and non-relapse mortality (NRM) offset any gains in disease control [2, 3].

The concept of Total Marrow Irradiation (TMI) targeting only haematopoietic tissue while sparing organs at risk was first proposed in 2001 at the City of Hope National Medical Center.4 This concept was extended to Total Marrow and Lymphoid Irradiation (TMLI), which additionally encompasses major lymph node chains and

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the spleen as targets, recognizing their role as sanctuary sites for lymphoid malignancy. The clinical application became possible with the widespread availability of advanced IMRT delivery systems in the early 2000s [4, 5]. The fundamental promise of TMLI to widen the therapeutic window by permitting dose escalation to sites of disease while protecting non-target organs has now been validated across multiple prospective phase I and II trials enrolling over 500 patients at leading transplant centers [4]. This review aims to provide the radiation oncologist and transplant team with a comprehensive understanding of TMLI: its scientific rationale, technical execution, clinical results, and the compelling case for its broader adoption.

2. Rationale: Why Move Beyond Conventional TBI?

2.1 Limitations of Conventional TBI

Conventional TBI is delivered using extended source-to-skin distance (SSD) techniques that irradiate the entire body relatively uniformly. While this approach is technically straightforward, it provides no flexibility to reduce dose to critical organs (beyond rudimentary lung shielding) or to selectively boost high-risk anatomical sites [6]. The lungs represent the primary dose-limiting organ; radiation pneumonitis has historically been reported in 10–85% of patients [1] The kidneys, liver, lenses, and gastrointestinal mucosa also receive full-body dose, contributing to a formidable late-effects profile including chronic kidney disease, hypothyroidism, and second malignancies. Moreover, the dose heterogeneity inherent in conventional TBI often ±10% across the body creates an unpredictable dosimetric landscape, rendering systematic dose escalation clinically unsafe. Lung blocks, the primary organ-sparing strategy in conventional TBI, are imprecise and can cause geographic miss of disease in mediastinal lymph nodes [6].

2.2 The Radiobiological Case for Targeted Escalation

There is a well-established dose-response relationship for radiation in leukemia and lymphoma. Escalating TBI dose from 12 Gy to 15.75 Gy in randomized trials demonstrated lower relapse rates, but at the cost of unacceptable NRM [3]. The recognition that the therapeutic window can be widened only if normal tissue dose is simultaneously reduced rather than merely keeping it constant forms the radiobiological core of the TMLI concept. TMLI achieves exactly this: it delivers escalated doses to bone marrow and lymphoid tissues (where disease resides) while actively reducing dose to non-target organs such as lungs, kidneys, liver, eyes, and oral mucosa [4, 5]. From an immunological perspective, TMLI also preserves its efficacy as a myeloablative and immunosuppressive tool. Bone marrow and lymphoid tissue are the primary targets of the immunosuppressive effect; by concentrating dose precisely where it matters, TMLI maintains conditioning efficacy while reducing collateral injury to immune-regulatory organs not involved in disease [7].

3. Technical Implementation of TMLI

3.1 Treatment Planning Systems and Delivery Platforms

TMLI is an IMRT-based technique and can be delivered via two principal platforms: helical tomotherapy (HT) and Volumetric Modulated Arc Therapy (VMAT) on a conventional linear accelerator [5, 8]. Helical tomotherapy, delivered on a TomoTherapy device, was the modality used in the pioneering trials at City of Hope. Its ability to treat the full body length in a single isocenter-free helical arc, with integrated megavoltage CT (MVCT) image guidance, made it ideally suited for the whole-body longitudinal target of TMLI [9]. VMAT-based TMLI on conventional linacs has subsequently demonstrated equivalent organ-at-risk (OAR) sparing and target coverage to HT-based delivery, with the practical advantage of being implementable at any center equipped with a modern linac capable of VMAT [5, 8]. Multi-isocenter VMAT approaches typically employ asymmetric jaws along the patient's longitudinal direction to cover different body lengths per isocenter. The lower extremities which have a relatively uniform cross-section and do not abut sensitive OARs are often treated with simple AP/PA fields on standard linacs [10]. Knowledge-based planning models have been developed to improve planning efficiency and consistency across diverse patient anatomies [11].

3.2 Patient Positioning, Immobilization, and CT Simulation

The entire body from skull to lower extremities must be imaged at CT simulation. Patients are typically simulated in two orientations head-first supine (HFS) and feet-first supine (FFS) with a junction zone at the mid-thigh level. Dedicated whole-body immobilization cradles and vacuum bags are used to ensure reproducibility. In institutions using helical tomotherapy, the patient (within the immobilization device) is physically rotated 180° between HFS and FFS plan delivery; junction dose is managed using complementary dose gradient overlaps between the two plans [9].

3.3 Target Volume Delineation

The clinical target volume (CTV) for TMLI encompasses the entire skeletal bone marrow (including the calvarium, vertebral bodies, sternum, ribs, pelvis, and long bones), the major lymph node chains (cervical, mediastinal, axillary, para-aortic, iliac, inguinal), and the spleen. The spinal canal a site of extramedullary relapse and CNS sanctuary is included in most protocols [7, 10]. In dose-escalated protocols delivering 20 Gy to skeletal marrow and lymph nodes, the brain and liver are dose-limited to 12 Gy to avoid unacceptable organ toxicity [10]. A key advantage over conventional TBI is the ability to individualize the target volume: boost doses can be delivered to sites of active or bulky disease (e.g., extramedullary lesions), and certain structures can be excluded (e.g., the mandible, to reduce mucositis) based on clinical judgment [4]. This level of spatial precision is simply unachievable with conventional TBI.

3.4 Dose Prescription, Fractionation, and Oar Constraints

In clinical trials, TMLI has been delivered at doses ranging from 12 Gy to 20 Gy, administered in twice-daily fractions of 1.5–2.0 Gy over 5 days (days −10 to −6 before transplant) [4, 12]. Prescription goal is typically to deliver 95% of the prescribed dose to 98% of the CTV, with dose heterogeneity maintained within 10% (Table 1) [9]. OAR constraints are prospectively defined for each protocol. The constraints mentioned in published series are: lungs ~9.1 Gy, kidneys ~7.3 Gy, gastrointestinal tract ~10.3 Gy, esophagus ~6.7 Gy, and oral cavity ~4.3 Gy representing 20–51% of the target dose (Table 2) [4]. These figures compare exceptionally favorably to conventional TBI where all organs receive the full prescribed dose. Daily image-guided verification (MVCT or CBCT) is mandatory before each fraction to ensure setup accuracy across the entire body length [9, 10].

3.5 Workflow Considerations and Resource Requirements

TMLI is a resource-intensive modality. Treatment delivery per fraction typically occupies the treatment machine for 90 - 180 minutes. Planning requires dedicated physicist time for multi-isocenter or helical arc planning, and close coordination between radiation oncologists, medical physicists, and the transplant team is essential [9]. Despite these demands, multiple centers have demonstrated that TMLI can be safely and robustly implemented with appropriate infrastructure and interdisciplinary collaboration [13]. The development of knowledge-based automated planning workflows is expected to reduce planning time and facilitate broader implementation [11].

4. Clinical Evidence: Efficacy and Safety

4.1 Relapsed/Refractory Acute Leukemia: Addressing an Unmet Need

The most compelling clinical data for TMLI come from patients with relapsed/refractory (R/R) acute leukemia, a population for whom standard conditioning regimens yield dismal outcomes. Historical data indicate that standard myeloablative alloHCT regimens, frequently in combination with TBI, yielded 1-year OS of only 29% for active AML and 28% for active ALL [14]. Stein et al. conducted the landmark Phase I trial at City of Hope enrolling 51 patients (age range 16–57 years) with R/R acute leukemia, escalating TMLI doses from 1200 cGy to 2000 cGy in combination with cyclophosphamide and etoposide [12]. The maximum tolerated dose was not reached at 2000 cGy the upper limit was set by lung dose approaching that of conventional TBI. NRM rates were 3.9% at day 100 and 8.1% at 1 year; 1-year estimated OS was 55.5%. All patients engrafted. A subsequent Phase II analysis of the first 57 patients with R/R AML (n=43) and ALL (n=14) treated with TMLI 20 Gy/cyclophosphamide/etoposide reported 1-year NRM of 6%, 2-year OS of 48%, and 2-year PFS of 33% outcomes that compare favorably to any published historical cohort for this disease state [4]. A Phase II trial (NCT02094794) is currently ongoing at City of Hope and continues to accrue patients [15].

4.2 Tmli in Standard-Risk And Complete Remission Disease

A critical recent development is the extension of TMLI from salvage/R/R settings to standard conditioning in complete remission. In a chemotherapy-free conditioning design, TMLI 20 Gy followed by post-transplant cyclophosphamide (PTCy) for GVHD prophylaxis was evaluated in AML in CR1/CR2 undergoing matched donor alloHCT. The 2-year outcomes were striking: OS 86.7%, relapse-free survival 83.3%, GVHD-free/relapse-free survival (GRFS) 59.3%, and NRM of 0% [4]. These results suggest that TMLI-based conditioning can achieve disease control equivalent to or superior to conventional myeloablative TBI while dramatically reducing NRM. Naik et al. recently reported outcomes of 58 patients (median age 20 years, including 20 children) with ALL undergoing matched sibling, unrelated, or haploidentical donor transplantation with TMLI and cyclophosphamide conditioning [13]. Engraftment was achieved in 96.5% at a median of 15 days. Sinusoidal obstruction syndrome occurred in 10 patients; hemorrhagic cystitis and cardiac dysfunction in 2 patients each. OS and DFS outcomes were comparable to historical TBI-based controls for matched sibling donors, while haploidentical outcomes were superior to fludarabine/busulfan-based myeloablative conditioning. This landmark report validates the feasibility and reproducibility of TMLI in the Indian subcontinent [13].

Table 1. TMLI Dose Prescription and Fractionation Schedule

Parameter	Adults	Children / Paediatric
Total prescription dose	15 Gy (standard) / 20 Gy (escalated protocols)	13.5 Gy
Fractionation	10 fractions, 1.5 Gy/fraction, twice daily × 5 days	9 fractions, 1.5 Gy/fraction, twice daily × 5 days
Timing relative to transplant	Days −10 to −6 before stem cell infusion	Days −10 to −6 before stem cell infusion
Inter-fraction interval	Minimum 6 hours	Minimum 6 hours
Coverage goal (CTV)	95% of prescribed dose to ≥98% of CTV	95% of prescribed dose to ≥98% of CTV
Dose heterogeneity	Within ±10%	Within ±10%
Brain mean dose	12 Gy (if CNS1/2; excluded from PTV)	As per protocol
Liver mean dose	≤12 Gy	≤12 Gy
Testis mean dose	≤12 Gy	≤12 Gy

Table 2. TMLI Organs at Risk (OAR) Dose Constraints

Organ at Risk (OAR)	Dose Constraint	Rationale
Lungs (bilateral combined)	Mean dose ≤ 7–8 Gy	Primary dose-limiting OAR; prevents radiation pneumonitis.
Heart	Mean dose ≤ 7–8 Gy	Reduce late cardiac toxicity.
Kidneys (bilateral combined)	Mean dose ≤ 5–6 Gy; PTV cropped from PRV Kidney (+2 mm)	Prevent radiation nephropathy.
Oral Avoidance Structure	Mean dose ≤ 5 Gy	Reduce oral mucositis; facilitates dose-escalated protocols.
Brain (CNS1/2 disease)	Mean dose ≤ 12 Gy (cropped from PTV)	Neurocognitive protection; leukocephalopathy prevention.
Liver	Mean dose ≤ 12 Gy	Prevent sinusoidal obstruction syndrome (SOS).
Testes / Ovaries	Mean dose ≤ 12 Gy	Gonadal function preservation where clinically appropriate.
Eyes / Lenses	Excluded from CTV; dose minimization	Cataract prevention.

4.3 TMLI in Elderly and Medically Unfit Patients

An important clinical niche for TMLI is the expanding population of older patients (≥50 years) or those with organ comorbidities who are ineligible for conventional myeloablative TBI. The organ-sparing capability of TMLI permits dose reduction to critical organs, allowing inclusion in a modified myeloablative regimen [7]. Rosenthal et al. reported on the seminal Phase I/II trial combining TMLI 12 Gy with fludarabine and melphalan in 33 patients with a median age of 55.2 years (range 12.2–68.4), specifically designed for those over 50 years or with compromised organ function precluding standard conditioning. Engraftment occurred in all patients at a median of 14 days. Long-term toxicities occurred in only 2 patients [16]. For the subgroup of patients ≥60 years treated with TMLI 12 Gy plus fludarabine/melphalan, 5-year OS of 42% was achieved with NRM comparable to fludarabine/melphalan alone demonstrating that the addition of TMLI does not increase toxicity even in this frail population [4].

4.4 TMLI in Haploidentical Transplantation

Haploidentical HCT with PTCy has revolutionized donor availability, but the platform carries a higher relapse risk due to the immunosuppressive effects of PTCy. The combination of TMLI with haploidentical HCT and PTCy was formally evaluated in a Phase I trial by Al Malki et al., enrolling 31 patients with high-risk and/or active primary refractory leukemia or myelodysplastic syndrome [17]. At 2000 cGy TMLI, 1-year relapse/progression rate was only 17%, with 1-year PFS of 74% and OS of 83% outcomes dramatically superior to historical haploidentical HCT data in comparable disease states [17]. Chronic GVHD at 2 years was 35%, and NRM remained low. These findings confirm that TMLI can be safely and effectively combined with the PTCy platform, potentially making haploidentical transplantation a more powerful curative option for high-risk disease. The Indian series from Vellore additionally reported that haploidentical transplant patients receiving TMLI achieved superior OS and DFS compared to historical controls receiving fludarabine/busulfan myeloablative conditioning, reinforcing the benefit of TMLI in this donor setting [13].

4.5 Tmli in Non-Hodgkin Lymphoma and Multiple Myeloma

TMLI has demonstrated applicability beyond acute leukemia. In evaluations of TMLI-based conditioning for allogeneic HCT in non-Hodgkin lymphoma, TMLI was specifically developed to deliver higher radiation doses to disease sites while reducing toxicity through organ sparing. Disease relapse occurring in 40–50% of NHL patients after alloHCT remains the primary cause of treatment failure, and TMLI's dose escalation potential offers a therapeutic advantage [6]. In multiple myeloma, the first-in-human use of TMI was pioneered in patients undergoing autologous tandem HCT, since myeloablative TBI added to high-dose melphalan was not feasible due to dose-limiting mucositis. TMI which spares the oral mucosa offered the opportunity to combine radiation and melphalan at full doses. Phase I/II trials using TMI doses up to 14 Gy with melphalan in relapsed multiple myeloma demonstrated complete response rates of 31% and transplant-related mortality of only 2% [18]. The organ-sparing feature of TMLI enables novel drug-radiation combinations previously deemed impossible with conventional TBI.

5. Toxicity Profile: the Key Advantage

5.1 Pulmonary Toxicity

Radiation pneumonitis is the most feared complication of TBI-based conditioning, historically occurring in 10–85% of recipients [1]. TMLI addresses this directly: lung doses in published TMLI series have consistently been lower than conventional TBI, explaining the observed low incidence of radiation pneumonitis across all trials [4]. In the City of Hope experience spanning over 500 patients, pneumonitis rates with TMLI have been consistently low. The mandible was deliberately excluded from the TMLI target volume in selected protocols to further reduce mucositis, which was the primary dose-limiting toxicity observed in conventional TBI/etoposide regimens [4].

5.2 Other Organ Toxicities

Analysis of patients undergoing TMLI demonstrates organ sparing translating to decreased clinical toxicities

including lower rates of nephrotoxicity, hypothyroidism, and cataract formation compared to conventional TBI [19]. In the Phase I trial of TMLI with cyclophosphamide/etoposide, despite treating patients with active leukemia at escalated doses, grade 3–4 non-hematologic toxicities were remarkably infrequent. Mucositis, the most common grade 3 toxicity, occurred in approximately 34% of patients lower than would be expected with TBI/etoposide at comparable doses [20].

The implications are profound for long-term survivorship. As HCT outcomes improve and more patients survive long term, the burden of chronic TBI-related late effects including secondary malignancies, endocrine dysfunction, cardiovascular disease, and neurocognitive impairment becomes increasingly important. The organ-sparing philosophy of TMLI addresses this prospectively, rather than treating sequelae after the fact.

5.3 Gvhd, Engraftment, and Non-Relapse Mortality

Across all published TMLI trials, engraftment rates have been uniformly high (>96%), with median neutrophil engraftment at 12–15 days comparable to conventional TBI-based conditioning [4, 13]. NRM rates, the most telling measure of conditioning-related toxicity, have been strikingly low in TMLI trials: 6% at 1 year in the R/R setting, 0% in AML in CR with PTCy, and 13% in the haploidentical PTCy setting [4, 17]. These figures challenge the conventional assumption that achieving myeloablative intensity necessarily implies high NRM. There is also emerging evidence that the intestinal dose delivered during TMLI does not significantly increase the incidence of acute GVHD, suggesting that the immunosuppressive efficacy of TMLI does not come at the cost of uncontrolled alloreactivity [21].

6. TMLI vs. TBI: A Direct Comparison

A formal randomized comparison of TMLI versus conventional TBI has not yet been conducted largely because the patient populations initially studied with TMLI (R/R, high-risk, elderly) are precisely those excluded from or poorly served by conventional TBI. Such a trial faces ethical challenges, given the favorable early-phase data for TMLI [22]. However, meaningful indirect comparisons are available. In the matched sibling donor ALL setting, Naik et al. demonstrated that OS and DFS outcomes with TMLI conditioning were equivalent to historical TBI-based conditioning in matched sibling donor transplants, while achieving this with substantially lower toxicity risk [13]. In the haploidentical setting, TMLI conditioning produced outcomes superior to standard fludarabine/busulfan myeloablative conditioning [13]. Dosimetric plan comparison studies consistently demonstrate that TMLI reduces mean organ doses to 20–51% of the target dose for all critical OARs, while maintaining full target coverage [10]. In contrast, conventional TBI delivers the full prescription dose to all organs. This dosimetric superiority of TMLI is not debatable; it is a physical reality. The clinical translation of this dosimetric advantage into improved patient outcomes lower toxicity, lower NRM, equivalent or superior disease control is increasingly well-documented.

7. Extramedullary Relapse after TMLI

A theoretical concern with targeted marrow irradiation is the potential for increased extramedullary (EM) relapse, given that non-targeted soft tissue sites receive lower radiation doses than with TBI. A retrospective analysis of five prospective TMLI trials involving 254 patients with R/R AML or ALL found that EM relapse rates after TMLI were comparable to rates reported with TBI and non-TBI conditioning regimens [23]. The inclusion of lymph node chains and the spleen in the TMLI target volume distinguishing TMLI from pure TMI is specifically designed to address sites of lymphoid sanctuary and reduce EM relapse risk. When EM relapse does occur after TMLI, it can be effectively salvaged with local radiotherapy. In the analysis by Dyk et al., radiotherapy directed at EM recurrence sites produced meaningfully better OS and PFS in patients with limited EM relapse, treated with curative intent [23]. This represents an additional advantage of the TMLI paradigm: prior TMLI conditioning does not preclude effective radiotherapy at relapse, since normal organ doses received during TMLI are substantially below re-treatment thresholds.

8. Future Directions

8.1 Expansion to Standard-Risk Disease and First Remission Transplants

Having demonstrated safety and efficacy in high-risk populations, TMLI trials are now proceeding to standard-risk disease in first complete remission. The chemotherapy-free TMLI/PTCy regimen reported for AML in CR is an exciting frontier, promising equivalent disease control with drastically reduced NRM and a simplified systemic regimen [4]. The FORUM trial has established TBI superiority over chemotherapy-only conditioning for paediatric ALL [24], TMLI, as a technologically superior form of TBI, is logically positioned as the next standard.

8.2 Proton-Based TMLI

The potential of intensity-modulated proton therapy (IMPT) to further reduce OAR doses in TMLI has been explored in dosimetric feasibility studies. IMPT capitalizes on the Bragg peak to deposit radiation dose with even greater spatial precision than photon IMRT, offering the theoretical prospect of further reducing lung, kidney, and heart doses. While currently limited to specialized centers, proton-based TMLI may eventually offer enhanced organ protection for pediatric patients and those with pre-existing organ dysfunction [25].

8.3 Automated Planning and Knowledge-Based Models

A major barrier to broader TMLI adoption is planning

complexity and time. Knowledge-based planning models leveraging prior plan databases to automate multi-isocenter TMLI planning have been developed and validated, demonstrating reduced mean doses to OARs and improved planning efficiency while maintaining plan quality [11]. Widespread availability of such tools will be essential for democratizing TMLI beyond high-volume specialized centers.

8.4 TMLI with Novel Immunotherapy Combinations

Current trials are exploring TMLI in combination with novel immune agents. The chemotherapy-free TMLI/PTCy platform at City of Hope has been augmented with nab-sirolimus for GVHD prevention, aiming to combine the powerful antileukemic effect of dose-escalated TMLI with minimized alloreactivity [23]. Such combinations, previously unexplorable with conventional TBI due to toxicity constraints, are now feasible within the TMLI framework.

9. Implementation Guidance for New Programs

Establishing a TMLI program requires close institutional collaboration between radiation oncology and the BMT team, ideally beginning with joint case conferences and a shared understanding of treatment goals. The following stepwise approach is recommended:

1. Infrastructure Assessment: A helical tomotherapy or VMAT-capable linac with online IGRT (MVCT or CBCT) is essential. Departments with a modern linac can implement VMAT-based TMLI.

2. Training and Simulation: Medical physicists and dosimetrists should receive dedicated training in whole-body CT simulation, multi-isocenter planning, junction management, and IGRT for TMLI. Close review of published technical guidelines is recommended.

3. Protocol Development: Institutional protocols should define target volumes, dose constraints, fractionation schedules, GVHD prophylaxis regimens, and supportive care measures in collaboration with the transplant team.

4. Prospective Data Collection: All patients treated with TMLI should be enrolled in institutional registries or prospective trials to contribute to the growing evidence base, particularly from the Indian subcontinent.

5. Collaboration: Institutions are encouraged to collaborate with established TMLI programs (nationally and internationally) for mentorship during the learning curve.

In conclusion, total Marrow and Lymphoid Irradiation represents a fundamental paradigm shift in the use of radiation as part of hematopoietic cell transplantation conditioning. By leveraging modern IMRT technology to deliver radiation where it is needed bone marrow, lymph nodes, and spleen while protecting where it is harmful, TMLI resolves the long-standing therapeutic dilemma of TBI: the inability to simultaneously achieve adequate disease control and acceptable toxicity.

The evidence base from over a decade of prospective clinical trials is compelling. TMLI achieves dose escalation to 20 Gy with 1-year NRM rates as low as 6% in R/R disease, produces OS and DFS equivalent or superior to conventional TBI in standard-risk disease, enables transplantation in elderly and medically unfit patients, and provides an ideal platform for haploidentical transplantation. The Indian experience from CMC Vellore has demonstrated that TMLI is not only a technology of academic centers in the United States it is implementable, safe, and effective in the Indian transplant setting [13]. TMLI is not the future of HCT conditioning it is the present. The question is no longer whether to adopt TMLI, but how quickly we can make this life-saving technology available to every patient who needs it.

Conflicts of Interest

The author declares no conflicts of interest.

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