Published in final edited form as:

Plast Reconstr Surg. 2015 March ; 135(3): 655e–656e. doi:10.1097/PRS.0000000000001108.

Helical Tomotherapy–Based Total Lymphoid Irradiation: A More Precise and Less Toxic Radiation Delivery System for Consideration in Composite Tissue Allotransplantation

Steve J. Kempton, M.D.,

Division of Plastic and Reconstructive Surgery

Frederick A. Robertson, M.D.,

Division of Anesthesiology

Michael L. Bentz, M.D., and

Division of Plastic and Reconstructive Surgery

Dixon B. Kaufman, M.D., Ph.D.

Division of Transplant Surgery, University of Wisconsin Hospital, Madison, Wis

Sir

Functional allotransplant tolerance can be achieved following the establishment of mixed donor and recipient hematopoietic chimerism by way of bone marrow or hematopoietic stem cell transplantation. Total lymphoid irradiation is an accepted adjunct to monoclonal and polyclonal antibody (chemotherapeutic) conditioning regimens before bone marrow transplantation that allows for successful donor cell engraftment into the recipient. These therapies have led to durable chimerism and complete immunosuppression elimination in solid organ transplantation patients.¹ The tendency in composite tissue allotransplantation, however, has been to substitute chemotherapeutic agents for total lymphoid irradiation because of concern for radiation damage to healthy “bystander” tissues.

The primary role of total lymphoid irradiation is to suppress the host immune system, a role that is shared with chemotherapeutic depletion. Recent studies have uncovered additional benefits of adding total lymphoid irradiation to chemotherapeutic regimens. Irradiation to lymphoid and bone marrow tissues may create a short-term local niche or “space” for donor cell engraftment, and enhance systemic engraftment in irradiated and nonirradiated tissues.² The addition of total lymphoid irradiation to chemotherapeutic depletion has been shown to provide a protective effect against development of graft-versus-host disease, and promote T-cell repopulation with a propensity toward a proregulatory immune system environment.³

Traditionally, total lymphoid irradiation is administered through the use of a linear accelerator with an anteroposterior opposed technique. This requires changes in patient

Correspondence to Dr. Kempton, Division of Plastic and Reconstructive Surgery, Department of Surgery, University of Wisconsin School of Medicine and Public Health, 600 Highland Avenue, Madison, Wis. 53792-3236, skempton@uwhealth.org.

DISCLOSURE

None of the authors has a financial interest in any of the products or devices mentioned in this article.

positioning and external shielding, and also subjects healthy tissues within the beam coverage to the prescribed radiation dose. In the past decade, radiation therapy technology has advanced toward more precise delivery methods. Image-modulated radiotherapy uses multiple low-dose radiation beamlets from multiple angles to allow for precise conformal therapy to tumor/target volumes and escalation of the dose without concomitant increase in normal tissue toxicity.

Helical tomotherapy represents the most recent advance in radiation therapy and combines image-modulated radiotherapy with modern megavolt computed tomographic image guidance. The added computed tomographic component allows for precise pretreatment planning, reconstruction of delivered radiation dose, and target registration to account for internal motion and volume changes. Importantly, helical tomotherapy allows for conformal avoidance (counterpart to conformal therapy), which specifically targets and avoids normal tissues. Multiple oncologic studies have shown that helical tomotherapy significantly decreases the radiation dose to bystander tissues, and can be used safely and successfully for total lymphoid irradiation.^{4,5}

Composite tissue allotransplantation immunosuppression minimization trials have been successful in reducing maintenance immunosuppression down to nonsteroid single-drug therapy. Helical tomotherapy offers a new method of radiation delivery that greatly reduces toxicity to normal tissues. The added tolerogenic effects of total lymphoid irradiation may help to overcome the stringent histocompatibility barrier seen in composite tissue allotransplantation. The protective effects of total lymphoid irradiation against graft-versus-host disease lowers patient risk and may allow for the infusion of a larger number of donor hematopoietic stem cell and T cells to achieve stable mixed chimerism. With success in both bone marrow and solid organ transplantation, total lymphoid irradiation should be considered in planning future animal and clinical composite tissue allotransplantation trials with the hope that it may move the science closer to reaching the common goal of immunosuppression elimination in composite tissue allotransplantation surgery.

References

1. Scandling JD, Busque S, Dejbakhsh-Jones S, et al. Tolerance and withdrawal of immunosuppressive drugs in patients given kidney and hematopoietic cell transplants. *Am J Transplant*. 2012; 12:1133–1145. [PubMed: 22405058]
2. Ito H, Takeuchi Y, Shaffer J, Sykes M. Local irradiation enhances congenic donor hematopoietic stem cell engraftment similarly in irradiated and nonirradiated sites. *Blood*. 2004; 103:1949–1954. [PubMed: 14592817]
3. Lowsky R, Takahashi T, Liu YP, et al. Protective conditioning for acute graft-versus-host disease. *N Engl J Med*. 2005; 353:1321–1331. [PubMed: 16192477]
4. Schultheiss TE, Wong J, Liu A, Olivera G, Somlo G. Image-guided total marrow and total lymphatic irradiation using helical tomotherapy. *Int J Radiat Oncol Biol Phys*. 2007; 67:1259–1267. [PubMed: 17336225]
5. McCutchen KW, Watkins JM, Eberts P, Terwilliger LE, Ashenafi MS, Jenrette JM III. Helical tomotherapy for total lymphoid irradiation. *Radiat Med*. 2008; 26:622–626. [PubMed: 19132495]