Hematol Oncol Clin N Am 20 (2006) 141–163
HEMATOLOGY/ONCOLOGY CLINICS
OF NORTH AMERICA

The Effect of Radiation Therapy on Normal Tissue Function

T.J. FitzGerald, MD*, Jesse Aronowitz, MD,
M. Giulia Cicchetti, MD, Graeme Fisher, MD,
Sidney Kadish, MD, Y.C. Lo, PhD, Charles Mayo, PhD,
Shelagh McCauley, MD, Joshua Meyer, MD,
Richard Pieters, MD, Alexandra Sherman, BS

Department of Radiation Oncology and the Cancer Center, University of Massachusetts Medical School, 55 Lake Avenue North, Worcester, MA 01625, USA

The influence of anticancer therapy on the health and function of normal tissue is complex. Combined medical and radiation therapies, both sequential and concurrent, are improving clinical outcomes with respect to tumor control, with enhanced patient survival and delay of recurrence. Therefore, more patients are at risk for treatment-associated sequelae of management. This evolving situation may be further exacerbated by the addition of new, targeted therapies. In patients who have breast cancer identified as having a demonstrated benefit to treatment with herceptin, the improvement in survival must be balanced against the heart damage associated with herceptin. The challenge to the radiation oncologist is to understand the potential acute and late morbidities associated with combined therapies and to use and further develop modern conformal radiation treatment techniques to limit or exclude normal tissue from the treatment field to decrease the risk of functional normal tissue injury.

During the course of external radiation therapy, treatment generally influences normal tissue function in tissues that have more rapid self-renewing proliferative index (eg, mucosal surfaces such as skin, head/neck, and esophagus) and other surface tissues that have more limited potential for self-renewal (eg, hair, nails, and surface glands). Injuries to these tissues are often self-limited and heal without specific intervention secondary to stem cell renewal. Acute effects from radiation therapy do not uniformly predict for late effects from treatment. Late effects generally affect tissues that have limited potential for self-renewal, and injury is often more permanent, requiring surgical débridement and possibly resulting in functional damage.

* Corresponding author. *E-mail address:* fitzgert@ummhc.org (T.J. FitzGerald).

0889-8588/06/$ – see front matter
doi:10.1016/j.hoc.2006.01.005

Table 1
Organ doses recommended for treating children who have intermediate-risk rhabdomyosarcoma

Organ	Dose Limit (Gy)
Kidney	14.4
Whole liver	23.4
Bilateral lungs	15.0 at 1.5 Gy/fraction
Whole brain ≥3 y	30.6
<3 y	23.4
Optic nerve and chiasm	46.8
Spinal cord	45.0
Gastrointestinal Tract (partial)	45.0
Whole abdomen-pelvis	24.0 at 1.5 Gy/fraction
Whole heart	30.6
Lens	14.4
Lacrimal gland/cornea	41.4

Courtesy of the Children's Oncology Group.

Children represent a special situation for normal tissue injury because each cell of a child has potential for self-renewal, and late effects develop at radiation doses that do not seem to result in acute or chronic effects in adults. More children have survived their primary disease, and radiation oncologists are beginning to investigate late normal-tissue effects of aggressive therapies. This knowledge becomes crucial to outcome as radiation oncologists begin to tailor therapies to balance the dichotomy of tumor control and late effects of treatment to normal tissue (Table 1). Although often not stated, the most discouraging late effect on normal tissue function is tumor recurrence, because secondary and

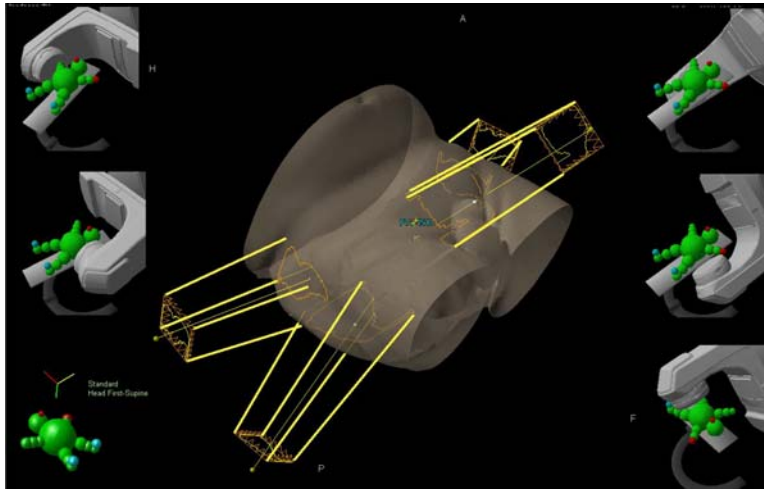

Fig. 1. Skin-rendering demonstration of non-coplanar geometry used to treat patients with adenocarcinoma of the prostate. The use of the anterior angled field augments dose to lymph nodes without additional radiation dose to the bladder and the sigmoid colon.