

The art and science of radiation therapy for gastrointestinal cancers

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The use of radiotherapy to treat gastrointestinal cancers has evolved in a gradual, step-wise fashion over the past six decades. By nature, gastrointestinal cancers are often diagnosed at a locally advanced stage. This fact, combined with the inherent sensitivity of most parts of the luminal gastrointestinal tract to high-dose radiation, has meant that radiation is often best used as part of a multimodality regimen, instead of as a sole curative modality. At times progress may have seemed modest and incremental, but when we look back, it is indeed remarkable how far we have come and how much our treatments have improved. We now have technology that allows us to extend life, cure disease while preserving critical organs, and ablate previously untouchable tumors.

The era of modern gastrointestinal radiation therapy arguably began in the 1960's, when investigators first combined fractionated radiotherapy with concomitant 5-fluoruracil (5-FU). This approach was ultimately carried forth into large cooperative group trials in rectal, pancreatic, gastric and other cancers, and showed benefit both in the adjuvant setting and as a definitive therapy (1-4). In the following two decades, investigators at Wayne State University discovered that chemoradiation with a combination of 5-FU and mitomycin C could be used as a non-surgical, organ-sparing option in the treatment of anal cancer (5), while RTOG 85-01 established that a subset of esophageal cancers could be cured by radiation combined with 5-FU and cisplatin, again without the need for radical surgery (6). In the 1990's, an elegant series of prospective studies at the University of Michigan brought important breakthroughs in the understanding of hepatic radiation tolerance (7). In conjunction with improvements in computers and linear accelerator technology, these

efforts bore further fruit in the 2000's, as prospective studies showcased the power and safety of stereotactic body radiotherapy (SBRT) for liver tumors (8,9). Most recently, we now have definitive evidence that preoperative chemoradiation improves survival in esophageal cancers over surgery alone (10). This list, by no means exclusive, highlights some of the major landmarks and turning points on our quest to overcome some of the most difficult-to-treat human cancers.

This issue reviews some areas of recent progress, new knowledge, and controversy in the field of gastrointestinal radiation oncology. In the first article, Dr. Lloyd and I explore the nuances that may allow us to enhance the therapeutic ratio of esophageal chemoradiation, now well established as a standard of care (11). Dr. Regine and colleagues then offer a masterful and balanced look at the very controversial area of adjuvant chemoradiation for pancreatic cancer (12).

The liver has traditionally been an organ that radiation oncologists have been hesitant to treat. The next two articles explore emerging therapies with great potential for local control of hepatic tumors. Dr. Kennedy, one of the preeminent authorities on hepatic radioembolization, offers a fascinating review of this very promising modality (13). Dr. Scorsetti looks at progress in liver SBRT, where remarkable advances in biological understanding and technology allow us to deliver treatment with previously unthinkable power and precision (14).

In the next section, Dr. Jabbour's team shares their expertise in the very technically demanding subject of radiation for anal cancers, where recent innovations with intensity modulated radiation therapy (IMRT) have led to significant therapeutic gains (15). Similarly, Dr. Sun Myint

and Dr. Kovacs demonstrate that techniques with a long history of use in rectal and anal cancer such as contact therapy and interstitial brachytherapy have been recently improved by technological developments. In expert hands, these techniques can be used to deliver to highly effective and personalized treatments with minimal morbidity (16,17).

With regard to the application of new radiation therapy techniques, gastrointestinal cancers offer some unique challenges and difficulties. Dr. Chen addresses the problem of organ motion, an issue that constantly threatens to degrade the radiation oncologist's therapeutic advantage, particularly in the abdomen (18). Dr. Lo leads a team of experts in an outstanding review of the tolerance of the gastrointestinal organs to the high-dose-per-fraction radiation that will be an increasingly important part of our anti-cancer arsenal (19).

There is actually a lot going on just below the surface in gastrointestinal radiation oncology. Doors have swung partly or fully closed on some indications, in that radiotherapy is no longer considered a primary part of treatment, or there are other options. Yet there are also new areas with incredible potential that we are just beginning to appreciate. Some of these techniques require new skills and many have steep learning curves. However, this should not dissuade us, nor should the ongoing need to perform the sometimes complex prospective trials needed to prove their value as we continue our search for the best possible treatments for our patients.

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