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The Red Journal's Top Downloads of 2013

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Although the number of citations a published paper receives over subsequent years tells us much about its enduring academic importance and clinical impact, there is nothing more immediate than studying the number of electronic downloads that papers receive to determine what is of importance to the radiation oncology community right now. The word "trending" has crept into Internet parlance to describe this up-to-the-minute monitor of the fluctuating interests of an audience. Over the last few years, the Red Journal has published a summary of its most downloaded papers from the previous year. These downloads are recorded by our publisher, Elsevier, via ScienceDirect, the publisher's library platform.

The Red Journal Editorial Board finds this information useful as we determine what is on the minds of practicing radiation oncologists, biologists, and physicists, and we feel it is also important for our readership to know where their interests are shared with others. In this article, we list the top 10 clinical downloads of 2013 together with the top 5 from both physics and biology.

It has been very striking to us how many of the papers downloaded thousands of times last year were featured not only in last year's list but also the year before (1-6). It is clear that a truly solid, highly relevant paper remains relevant for more than just a year and that this, perhaps, should not be too surprising as good science should never be just a flash in the pan.

Looking at the top 10 clinical downloads, we see, again, a craving for radiation oncologists to practice their art within an evidence-based framework. Every single one of these papers is a guideline, consensus statement, a prospective trial, or a meta-analysis. Although smaller studies that are retrospective in nature or based in a single institution may occasionally generate a novel hypothesis, they

Clinical

Rank	Article	(ref)
1	Marks LB, et al 2010. Use of Normal Tissue Complication Probability Models in the Clinic.	(7)
2	Lim K, et al 2011. Consensus Guidelines for Delineation of Clinical Target Volume for Intensity-Modulated Pelvic Radiotherapy for the Definitive Treatment of Cervix Cancer.	(8)
3	Hall WH, et al 2008. Development and Validation of a Standardized Method for Contouring the Brachial Plexus: Preliminary Dosimetric Analysis Among Patients Treated With IMRT for Head-and-Neck Cancer.	(9)
4	Sperduto PW, et al 2013. A Phase 3 Trial of Whole Brain Radiation Therapy and Stereotactic Radiosurgery Alone versus WBRT and SRS With Temozolomide or Erlotinib for Non-Small Cell Lung Cancer and 1 to 3 Brain Metastases: Radiation Therapy Oncology Group 0320.	(10)
5	Kong FM, et al 2011. Consideration of Dose Limits for Organs at Risk of Thoracic Radiotherapy: Atlas for Lung, Proximal Bronchial Tree, Esophagus, Spinal Cord, Ribs, and Brachial Plexus.	(11)
6	Lutz S, et al 2011. Palliative Radiotherapy for Bone Metastases: An ASTRO Evidence-Based Guideline.	(12)
7	Specht L, et al 2013. Modern Radiation Therapy for Hodgkin Lymphoma: Field and Dose Guidelines from the International Lymphoma Radiation Oncology Group.	(13)
8	Gay HA, et al 2012. Pelvic Normal Tissue Contouring Guidelines for Radiation Therapy: A Radiation Therapy Oncology Group Consensus Panel Atlas.	(14)
9	Kachnic LA, et al 2013. RTOG 0529: A Phase 2 Evaluation of Dose-Painted Intensity Modulated Radiation Therapy in Combination With 5-Fluorouracil and Mitomycin-C for the Reduction of Acute Morbidity in Carcinoma of the Anal Canal.	(15)
10	Palma DA, et al 2013. Predicting Radiation Pneumonitis After Chemoradiation Therapy for Lung Cancer: An International Individual Patient Data Meta-analysis.	(16)

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Physics

Rank	Physics	(ref)
1	De Los Santos J, et al 2013. Image Guided Radiation Therapy (IGRT) Technologies for Radiation Therapy Localization and Delivery.	(18)
2	van Herk M, et al 2000. The Probability of Correct Target Dosage: Dose-Population Histograms for Deriving Treatment Margins in Radiotherapy.	(19)
3	Ling CC, et al 2008. Commissioning and Quality Assurance of RapidArc Radiotherapy Delivery System.	(20)
4	Feuvret L, et al 2006. Conformity Index: A Review.	(21)
5	Bedford JL and Warrington AP. 2009. Commissioning of Volumetric Modulated Arc Therapy (VMAT).	(22)

rarely define the practice of radiation oncology and have never been featured in any of our top 10 lists.

The most downloaded article remains the summary paper from the Quantitative Analysis of Normal Tissue Effects in the Clinic (QUANTEC) analysis by Marks et al (7) published in 2010. This project represented a huge shift in the way we as a specialty think about morbidity and its risk and was a quantum leap upward in sophistication from the important work of Emami et al (17) in the 1990s, which had previously described our relationship with normal tissues. We expect this work will remain essential reading for many years to come.

In keeping with our new understanding of normal tissue risk comes the critical need to define normal structures as accurately as we can in our treatment planning process. Thus, we find consensus guidelines, anatomic atlases, and validated contouring techniques are very prominent in this list (8, 12, 14). The urgency of the need to cover the entire human body structure-by-structure and region-by-region is reflected in the fact that many different societies and individual institutions are involved in the effort. We see pelvic contouring guidelines from the Radiation Therapy Oncology Group (RTOG) (10, 15) and Hodgkin lymphoma field design from the International Lymphoma Radiation Oncology Group (ILROG) (13). We also see expert consortia defining anatomy and dose limits for thoracic structures and for the brachial plexus (9, 11). New data to assist in modeling and defining normal tissue tolerance are represented by a new meta-analysis from Palma et al (16) defining the predictors of pneumonitis after chemoradiation therapy for lung cancer.

As well as defining and understanding the normal tissues, we must also understand and best use the novel imaging that now defines our tumor target volumes. As imaging improves, target volumes and margins shrink. This creates a sense of unfamiliarity and unease among practitioners, who worry about geographic misses. The GYN IMRT Consortium first wrote their clinical target volume definitions for cancer of the uterine cervix in 2010, and this remains our second most-downloaded paper 3 years later (8).

Both of the novel prospective studies that have entered the top 10 list come from the RTOG. The first is a phase 3 trial of whole-brain radiation therapy (WBRT) and stereotactic radiation surgery (SRS) alone versus WBRT and SRS with temozolomide or erlotinib for non-small cell lung cancer and 1 to 3 brain metastases (RTOG 0320) (10); and the second study is a phase 3 evaluation of dose-painted IMRT in combination with 5-fluorouracil and mitomycin-C for the reduction of acute morbidity in carcinoma of the anal canal (15). Both of the studies show the desire to rapidly learn how to integrate our new technologies (SRS and IMRT dose painting) with both new and old systemic therapies. The American Society for Radiation Oncology (ASTRO) guidelines for the use of radiation for bone metastases is another document that is likely to have enduring relevance as radiation oncologists nervously move from multifraction to single-dose treatments under the weight of the evidence and look to the specialty societies to give them cover.

The physics category makes very interesting reading, with 2 articles featured last year that are featured again, demonstrating lasting relevance. The first article, by van Herk et al (19), is more than a decade old and has been heavily cited. It describes a simple methodology to determine margins from clinical target volume (CTV) to planning target volume (PTV) and the probability of CTV receiving the prescribed dose. It can be used for different tumors at different sites and has become the yardstick against which all new methodologies are measured. The second paper, a critical review by Feuvret et al (21), reports different methodologies available to evaluate coverage in treatment plans. As our treatment becomes increasingly complex so to does our need to have a mutually agreed upon conformity index that takes into account heterogeneity of coverage as well as adequacy of target, and normal tissue dosing becomes more critical.

Three new papers step up into the top-5 category. An ASTRO white paper on image-guided technologies available for radiation treatment delivery is now number 1 (22).

Biology

Rank	Biology	(ref)
1	Herbst RS. 2004. Review of Epidermal Growth Factor Receptor Biology.	(23)
2	Zeng J, et al 2013. Anti-PD-1 Blockade and Stereotactic Radiation Produce Long-Term Survival in Mice With Intracranial Gliomas.	(24)
3	Wang C and Lees-Miller SP. 2013. Detection and Repair of Ionizing Radiation-Induced DNA Double Strand Breaks: New Developments in Nonhomologous End Joining.	(25)
4	Stamell, EF, et al 2012. The Abscopal Effect Associated With a Systemic Anti-melanoma Immune Response.	(26)
5	Brown JM, et al 2013. Dose Escalation,Not "NewBiology," Can Account for the Efficacy of Stereotactic Body Radiation TherapyWith Non-Small-Cell Lung Cancer.	(27)

This will become an important reference work for this rapidly developing field, and it is hoped that it will be regularly updated. The remaining 2 papers describe the commissioning and quality assurance of volumetric modulated arc therapy. This technology is being taken up rapidly in the clinic as it would appear to provide the precision and dose optimization of IMRT but with shorter treatment times. These how-to papers are important for the safe implementation of a complex technology across a wide range of treatment facilities (21).

Among the biology category articles is a review of the epidermal growth factor that remains the most downloaded paper, a clear sign of the importance of understanding the receptor and its associated pathways in contemporary cancer therapy (23). The paper by Wang and Lees-Miller (25) on radiation-induced double-strand DNA breaks and new developments in nonhomologous end-joining repair mechanisms has proved to be popular, and, we suspect, beyond just the radiation oncology community. DNA repair is widely important in oncologic therapy, broadening the appeal of the paper. Programmed death 1 (PD-1) is a membrane protein known to be involved in the regulation of immune cell differentiation that can now be targeted by monoclonal antibodies. Clinical responses have been seen in melanomas, and it is currently being tested with great excitement across treatment of a wide range of cancers. It is, therefore, unsurprising to see the paper by Zeng et al (24) investigating the combination with SRS for treatment of murine gliomas drawing interest. Another paper, by Stamell et al (26), investigating the abscopal effect in melanoma further illustrates how this disease is providing new paradigms in cancer therapy. Finally, a contentious debate in our field is whether the undoubted benefits of SRS derive simply from the high biological doses, from radiation delivered, or from a new biology unleashed by these doses, (eg, unique vascular effects or the exposure and liberation of tumor antigens). Brown et al (27) have stoked the flames of the debate with a review article, concluding that there is no new biology, but I suspect we have not heard the last of this issue.

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