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COMMENTARY

Underrepresentation of Local Therapy Trials in Leading Medical Journals: Cause for Outrage or Indifference?

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Two academic radiation oncologists walk into a bar. Exasperated Investigator (EI) slumps down and orders a stiff drink while Indifferent Editor (IE) sidles up next to him, exhorting the barkeep to whip up something tropical. Head down, arms encircling his martini, EI conveys by his body language that the sky has indeed fallen, and now we have proof. IE is anxious to get the night going, but sensing his colleague's despondency, gives him a gentle pat on the shoulder.

IE: Good to see you again, EI. What's got you down? You're looking a little glum.

EI: Nothing much. It's just...I read this article by Holliday et al today in the Red Journal.

IE: Sorry. Haven't had time to read it. Lots of manuscripts to handle, you know. What's it about?

EI: It's a study that confirms my long-held suspicion that the top journals are out to get our specialty.

IE: You sound like a conspiracy theorist.

EI: Well, data are data. But you are quite perspicacious. There *is* something else bugging me.

IE: Oh yeah?

EI: Yes. I recently had a manuscript rejected from *JAMA*. See?

(Holding up his iPhone to show the offending e-mail)

IE: I'm sorry to hear that. Was it a large practice-changing randomized trial?

EI: Not really.

IE: Oh? It must have been an important and timely meta-analysis?

EI: It was a case report...

IE: I see.

EI: ...on the bystander effect in a zebrafish model. It was really quite a clever experiment.

IE: I bet. Well, don't get out of control tonight. You know, there's a new mood-stabilizing drug out that might interest you. I read about it the current *New England Journal*.

EI: You're not helping. Fortunately, my paper is presently under review by *JAMA Medical Waste*.

IE: Oh yeah? *JMW*? I love that journal. They publish great stuff. You know, if you hold your thumb over the last two words, it's as good as a *JAMA* article.

EI: I just mumble the part after *JAMA*.

IE: Even better. So what about that Holliday article you were talking about?

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Conflict of interest: none.

EI: Well, the authors analyzed 960 articles and showed that local therapy trials are less likely to get published in leading journals, *ceteris paribus*.

IE: That sounds painstaking. You know, some colleagues and I talked about doing a study like that years ago. We could never get funding for it, though. I'm intrigued—tell me more.

EI: I'm too upset to talk about it.

IE: Aw, don't be so taciturn. The night is young. There are two sides to every debate, just like climate change, evolution, or vaccination. I have my prejudices, but enlighten me; I'm willing to listen. It'll help to talk about your feelings.

EI: All right; you asked for it.

In this issue, Holliday et al (1) present a bibliometric analysis of oncologic publications in the scientific literature. They found that local therapy trials are underrepresented in leading medical journals compared with trials of systemic therapies. Oncology necessitates a multimodal therapeutic approach to ensure quality patient care. Leading journals possess an influential role in disseminating new research findings, given their large readership. Underrepresentation of local therapies in these journals marginalizes their role in exchange for increasing emphasis on systemic therapies. Consequently, medical oncologists may be unaware of new radiation therapy indications or advancements. Furthermore, publication in high-impact journals is frequently used as a marker for scientific excellence and academic promotion.

Despite these implications, it is uncertain whether leading journals are concerned about adequately representing the various branches of oncology. Editors have multiple responsibilities, including emphasizing important advancements, ensuring scientific rigor, and producing content of interest to subscribers—of whom a minority are radiation oncologists. Examining factors predicting publication in leading medical journals can help reveal disparities. On multivariable analysis, Holliday et al found that systemic intervention, randomized design, sample size, metastatic setting, and hematologic malignancy were associated with appearance in leading medical journals. Interestingly, there was no difference between systemic and local therapy trials regarding randomization, significance of the primary endpoint, or using survival as the primary endpoint. Despite local therapy trials being superior to systemic therapy trials in terms of larger sample sizes and longer follow-up times, systemic trials enjoyed greater representation in leading medical journals.

One potential explanation is the increasing emphasis on personalized medicine (2). Enthusiasm for new mechanisms to treat cancer, coupled with potential financial gain for pharmaceutical companies, has led to a dramatic increase in targeted therapy trials. Others have shown that

such trials are more likely to have industry funding compared with local therapy (3). Meanwhile, industry-sponsored studies are more likely to use surrogate endpoints and short follow-up times. This model is well suited for quickly bringing drugs to market, and it may be necessary to expedite approval of novel therapies; however, continued recognition of the significance of advancing local cancer therapies is essential, too.

Underrepresentation of local therapy trials represents a form of publication bias, influenced by research topic, rather than study design. One strategy to minimize “topic bias” would be to adopt objective scoring criteria—for example, prospective design, blinding, randomization, endpoint, and length of follow-up—to grade a study's rigor and standardize the review process. Such a system could be implemented along with a subjective component that includes impact, applicability, and timeliness. It would be worrisome, for example, if journals consistently published lower-scored studies only to promote a particular area of research.

The small size of the radiation oncology specialty poses challenges, both in adequately representing its research in the mainstream scientific literature, and in obtaining funding (4). With the federal budget for cancer research declining, industry-funded studies are playing an increasingly dominant role in sponsoring clinical trials. Novel radiation therapy technologies are attractive strategies for advancing patient care, but clinical trials may be perceived as unnecessary for their marketability or profitability, in contrast to new drugs. This makes for a challenging funding climate in radiation oncology, particularly when we consider the disproportionate lack of federal funding (4). Increasing awareness of such biases is needed to ensure adequate representation of local therapies in scientific literature.

IE: You make a strong case. I'm still not convinced this matters, but I'll grant you raise some valid concerns, especially the enlarging influence of industry. I've always considered industry-funded science an oxymoron, since it's science with an agenda.

EI: Talking about it has made me feel worse. I think I'll take you up on that antidepressant.

IE: Now, now. Momentarily. First, hear me out. I've got some tough love for you, with a trace of optimism.

First, cry me a river. *Ceteris ain't paribus*. Editors have every right to choose what they publish. It's not a court of law. Publishing science isn't meant to be scientific. What you're calling topic bias looks to me like editor's discretion. Let's get to the heart of it. You just want your ego massaged by publishing in a prestigious journal. So get over yourself. This isn't about you. Publications are not ends. They are means to help patients by disseminating truth. If your research is worthy, it will get published, and you'll get promoted. If you're disappointed by its publicity, pound a

drum. Post to YouTube. Tweet. Times have changed. Most people are reading this editorial via download, not print. If you want a big audience, go make action movies, and leave radiation sciences to the rest of us.

Second, I think you have a lofty ideal of medical journalism. Most of what is published in leading medical and science journals has zero impact on our research or on our patients. So what if you published a paper in a journal that has a high impact because people in other specialties quote its articles that are unrelated to yours? This has no bearing on anything substantive. I'll prove it by referencing a *Science* study on political preferences (5). There, I just increased their impact factor. Take that, *Nature*!

Third, does an internist really need to know immediately that 80 Gy has a survival advantage over 70 Gy? Medical oncologists aren't looking over our shoulders when we write prescriptions. Some trials seem just right for a specialty journal. Maybe it *is* more interesting for the wider community to hear that cutting-edge targeted therapies are working against refractory cancers. Who are we to judge? Great science can also be really boring. Nothing you'd put above the fold and stand on a street corner yelling "Extra!" Plus, boring is in the eye of the beholder. As Hofstadter once remarked in his glorious, excellent book (6):

*Meaning lies as much
in the mind of the reader
as in the haiku*

So judge the science for yourself, and quit worrying about who published it.

EI: My friend, I don't share all your views, but I am actually feeling better after your long-winded rant. I don't think I'll need those psychiatric meds after all.

IE: That's more like it. Now, let's have a good time. And cheer up about your case report. If *JMW* won't take it, I know a journal that published one on the abscopal effect not that long ago.

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