Suggestions for topics suitable for these Point/Counterpoint debates should be addressed to Colin G. Orton, Professor Emeritus, Wayne State University, Detroit: ortonc@comcast.net. Persons participating in Point/Counterpoint discussions are selected for their knowledge and communicative skill. Their positions for or against a proposition may or may not reflect their personal opinions or the positions of their employers.

Increasing dependence on industry-funded research creates higher risk of biased reporting in medical physics

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OVERVIEW

When companies fund research they obviously hope that the research will demonstrate the superior effectiveness of their products. Consequently, publication of negative results might make companies less enthusiastic about supporting such research in the future. Since researchers who use industrial support are likely to be eager to continue with this funding, some believe that this might increase the risk biased reporting. This is the premise debated in this month’s Point/Counterpoint.

Arguing for the Proposition is Sonja Dieterich, Ph.D. After completing her Ph.D. in Nuclear Physics at Rutgers University in 2002, Dr. Dieterich received training in Medical Physics at Georgetown University Hospital, Washington DC, from 2002 to 2003. In 2003, she accepted a faculty position at Georgetown. From 2007-2012, she worked at Stanford University Hospital as Clinical Associate Professor and Chief of Radiosurgery Physics. Currently she is an Associate Professor and Physics Residency Co-Director at the University of California Davis. Dr. Dieterich is Chair of the AAPM Task Group 135 "QA for Robotic Radiosurgery" and a member of the ASTRO Physics and Multi-
Disciplinary QA Committees. Her current research interests are the development of QA/QM programs for new technologies, image-guided brachytherapy, and veterinary radiation oncology.

Arguing against the Proposition is Paul J. Keall, Ph.D. Dr. Keall is a Professor at the University of Sydney in Australia. His work is broadly supported by the NHMRC Australia Fellowship *Innovations in Medical Physics to Improve Human Health* with additional funding supporting individual projects from Australian and US government sources. Prof. Keall’s main scientific interests involve image-guided radiation therapy and accounting for anatomic and physiologic changes in healthy and pathologic tissue throughout a radiation treatment course. Additional areas of investigation include ventilation imaging, audiovisual biofeedback, and MRI-guided radiotherapy. These research activities have resulted in over 170 scientific articles and several awards and honors. He has developed new methods for medical imaging and image-guided radiation therapy that have been translated into clinical practice. Relevant to this debate, and in the full disclosure spirit of TG109, to quote Rock Mackie “Dr. Keall is a poster-child for conflict-of-interest”, having held over 20 research agreements with start-up, mid-size and large companies along with awarded patents and commercial licenses.

**FOR THE PROPOSITION: Sonja Dieterich, Ph.D.**

**Opening Statement**
As humans, we are hard-wired toward implicit bias. The Washington Post published on biased reporting in pharmaceutical research, which triggers some self-examination about potential publication bias in medical physics. Let us assume that vendors and researchers have been able to avoid conscious bias exerted by pressures of market shares and up-or-out research faculty appointments which depend on securing ever scarcer grants. The issue of implicit bias still remains. To conduct good science, we must address all factors affecting the quality of science; publication bias is a major known factor to affect research quality, and with shrinking NIH budgets will only gain in influence.

A large body of research is available on publication bias. To summarize: (1) there is publication bias in medical journals toward positive outcomes, (2) the incidence of editors or reviewers rejecting negative studies is small for JAMA, but unknown for most other journals, and (3) published reports from industry-funded studies show a larger bias toward positive results. Unless medical physics journals (e.g. Medical Physics, PMB, JACMP) publish data to the contrary, my working hypothesis is for an existing editorial/reviewer bias of unknown size toward rejecting papers which report negative study outcomes. No reviewer guideline, journal review submission websites or our Code of Ethics addresses implicit bias toward positive study outcomes.

One proposed way to remove positive publication bias is to require all federally funded-research to be published independent of outcome, provided the scientific method and statistical analysis meet quality standards. It remains to be seen if industry would commit to this solution as well because, for such a commitment to be meaningful,
vendors would need to provide means of independent verification such as a publicly-accessible listing of all outside research contracts.

Increased reliance on industry funding also increases the risk for comparative effectiveness research on technology to remain unfunded. Few institutions can afford the cost and redundancy of operating two or more technologies designed to perform the same function. For vendor-funded research, there is no incentive to compare clinical effectiveness of competing technologies. Instead, the implicit bias is toward research on the new technology vs. older technology. One clinical example is respiratory motion compensation. Several vendors provide solutions for each of the four techniques: compression, breath-hold, gating, and real-time tracking. Despite the widespread acceptance of these technologies and a large variation of cost to implement and use them, there is not a single prospective clinical trial which would provide data on patient outcomes based solely on the technology used for treatment.

AGAINST THE PROPOSITION: Paul J. Keall, Ph.D.

Opening Statement

As scientists we have a mandate to generate new scientific knowledge. As medical physicists we perform and publish work that can improve how we detect, image, diagnose and treat disease. However, our academic integrity struggles against biased reporting for any publication independent of its funding source: we have an inherent self-interest in having articles published that help us get and keep grants, help with promotion
and career prospects, help with invitations to give talks at interesting places, and many other benefits. As a result, for many reasons, a few of us ‘behave badly’.  

Industry-funded research plays an important role in improving health outcomes, typically supporting medium-to-late stage research aligned with product roadmaps. Often late-stage research requires engineering support to allow clinical testing that otherwise would not be possible. The potential for conflicts-of-interest exist. Fortunately, to avoid any undue influence of industry pressure on the outcomes of research, there are a number of mechanisms to protect and isolate researchers from external influences and therefore reduce the risk of biased reporting. Three protection mechanisms reducing the risk of biased reporting are: (1) increased accountability from medical journals regarding ethics and conflicts of interest, (2) greater academic freedom in industrial-university agreements and (3) stronger governmental regulation of commercially-sponsored research.  

(1) Increased accountability from medical journals regarding ethics and conflicts of interest  

All reputable medical journals now have conflict of interest policies. Many journals follow the ICMJE conflict-of-interest policy in which each author must submit a written signed disclosure. *Medical Physics* requires that “Each author of a manuscript is required to disclose any and all potential conflicts of interest that could be perceived to bias the results reported in the manuscript.” This policy raises awareness for authors submitting the work, reviewers and readers, and increases authors’ accountability.
(2) Greater academic freedom in industrial-university agreements

Over time, universities have taken a much stronger stance with respect to research conduct and publication control. An example from a University of Sydney agreement states: “As a matter of basic academic policy, the University retains the right to publish in its discretion material relating to the conduct and conclusions of the Research”, meaning that the academic staff have the right to publish and interpret their own results without industry direction or oversight.

(3) Stronger governmental regulation of commercially sponsored research

The US FDA, NIH and other government bodies have a vested interest in ensuring that publications of studies represent the actual results. There is new and proposed regulation for conflicts of interest, assessing conflicts prior to the start of a study to potentially recuse investigators, avoid data falsification, and provide data storage and data access. An as example, NIH policy states: “This complexity, as well as a need to strengthen accountability, led to changes that expand and add transparency to Investigators’ disclosure of Significant Financial Interests (SFIs), enhance regulatory compliance and effective institutional oversight and management of Investigators’ financial conflicts of interests.”

In summary, medical journals, universities and governments are actively working to protect investigators from external influences and therefore decrease the risk of biased reporting in journals such as *Medical Physics*.

Rebuttal: Sonja Dieterich, Ph.D.
Dr. Keall highlights the increased efforts to address biased reporting in science. The questions we need to evaluate are: How effective are we in enforcing these rules, and have we done enough to cause a change in our culture? To use an analogy, the posted speed limit is the rule, but the unwritten culture (on most highways in the USA, Germany and Australia at least) is for traffic to proceed at 10 miles-per-hour above the posted speed limit without fear of repercussion by the highway patrol.

Dr. Keall cited a very good paper published in 2005, which I have examined for data pertaining to funding source influence on outcome reporting, i.e. violation of scientific integrity standards. Table 1, entry 10 in this paper lists the incidence of “Changing the design, methodology, or results of a study in response to pressure from a funding source” as 15.5% on average (9.5% for early career and 20.6% for mid-career scientists). Given that the study plausibly argues the under-reporting of results, these percentages hardly constitute just a few of us behaving badly, as my opponent states. I was unable to find data suggesting this percentage had decreased with the implementation of the three protection mechanisms Dr. Keall listed.

To be effective in making science less prone to bias, the interventions must (1) remove the motivation for biased behavior, (2) implement a means of identifying researchers who do not follow scientific standards, and (3) increase the stakes for being found in violation of scientific standards. None of the three interventions listed by Dr. Keall remove the motivation for biased behavior. Indeed, decreasing support through outcome-neutral funding sources has increased the pressure. The second intervention, greater freedom to publish, looks good on paper but in reality will not protect the
researcher from losing continued industry sponsorship should negative outcome reporting be undesired by industry.

In summary, while gross scientific misconduct through fabrication, falsification and plagiarism is indeed committed by very few of us, I (pessimistically) maintain that our scientific culture has not yet changed sufficiently to remove the significant pressure towards biased reporting. We neither have data to allow us to make a conclusive statement that biased reporting is not an issue, nor do we have any auditing procedures in place to raise the stakes for breaking the rules.

Rebuttal: Paul J. Keall, Ph.D.

Dr. Dieterich has some very good points and suggestions to improve the amount of negative-result research being published and the impact of declining Federal funding on clinically important research, such as comparative effectiveness studies. She asserts that (1) humans are subject to bias, (2) there is evidence supporting publication bias, (3) Federally funded (and ideally industry-funded) research be published regardless of positive/negative results, and (4) the impact of increased reliance on industry funding means that some important research areas are unfunded. These observations are all valid. However, they do not lead to the conclusion that increasing dependence on industry-funded research creates higher risk of biased reporting in medical physics. Moreover, several of the references used to support her statement pertain to the pharmaceutical world; none specifically address biased reporting in medical physics research.

To further the debate, the pathway to impacting patients on a large scale is necessarily through industry. Having ideas proceed from bench to bedside is one of the
most rewarding professional accomplishments in our field. Academic/industrial interactions are essential for this translational research. AAPM TG109\textsuperscript{6} states “There is nothing inherently wrong with a conflict of interest, but it should be acknowledged to eliminate the perception of possible impropriety. The best protection against conflict of interest accusations is full disclosure and the acquisition, interpretation, and publication of research findings in a manner that is transparent and above suspicion.” To navigate these interactions, in addition to the three protections reducing the risk of biased reporting detailed in my Opening Statement, researchers receive ethics education throughout their lives, along with a growing ethics component of graduate\textsuperscript{8} and residency\textsuperscript{9} medical physics programs and in our profession.\textsuperscript{6}

References

1 Project Implicit [https://implicit.harvard.edu/implicit/demo/]


