Editorial

Surgical Translational Research May Be Forward or Reverse

Abstract: The classic concept of translational research can be described as a bench-to-bedside approach. Reverse translational research, bedside-to-benchtop, also may have a place. Under some circumstances, innovative clinicians may develop new techniques in advance of basic science research. A recent example of the success of reverse translational research is shoulder superior capsular reconstruction. Theoretically, new surgical techniques are ideally first tested ex vivo, but this does not guarantee clinical success, and in some cases, experienced, specialized surgeon-scientists can modify existing techniques and perform novel interventions with little risk to patients. Benefits of reverse translational research include a shorter time from innovation to application, and real, not theoretical, determination of clinical outcome. If a reverse approach is warranted, strict adherence to bioethical principles is required, including cooperation with ethics committees, institutional review boards, trial registration, and informed consent. Translational research can be bidirectional.

Translational research connotes a bench-to-bedside approach with an aim to translate basic science or laboratory analysis to clinical application. Novel therapeutic and interventional treatments entail unknown outcomes and risks in human subjects and are ideally tested in the laboratory with a goal of first trying to understand how patients may respond.[1,2] Translational research is a 2-way street, and feedback from clinicians to scientists is important.[2,3] In addition, basic research is sometimes poorly understood by clinicians, and vice versa.[2] Thus, a team approach to biomedical research is needed, and under some circumstances, clinicians, including the innovative readers of *Arthroscopy*, develop new techniques in advance of basic science research.[4]

Some have reported a decline in basic science research reporting in the biomedical literature,[5] yet in our clinical journal, *Arthroscopy*, approximately 20% of what we publish is characterized as "basic science." However, the ratio of basic science to clinical studies published does not describe "Which came first?" The direction of translational research may be forward…or it may be in reverse.

A recent example of reverse translational research is shoulder superior capsular reconstruction (SCR). The concept was popularized by Mihata et al.,[6] who published a basic science study investigating the concept in 2012. One year later, the results of SCR were published[7] with clinical follow-up as long as 51 months; in addition, Mihata et al.[8] published clinical outcomes of SCR in a Japanese journal in 2010. It could be possible that basic science investigation came first, and publication lagged, but it appears that reverse translational research was the case, i.e., clinical treatment before basic science investigation. This is not necessarily a bad thing; SCR shows successful outcomes.[9-13]

Translational research may flow in forward or reverse. Theoretically, new surgical techniques are ideally first tested ex vivo.[14-18] However, ex vivo results do not guarantee clinical success, and in some cases highly specialized and experienced surgeon-scientists can modify existing techniques and perform novel interventions with very little risk to their patients and great potential benefits.

Benefits of reverse translational research may include a shorter time from innovation to application, and real, as opposed to theoretical, determination of clinical outcome. That said, health care ethics require proper informed consent, helping patients, avoiding harm, and just and equal treatment of patients regardless of race, gender, religion, education, or social status.[19] Reverse translational research does entail risk, and we surgeon-scientists must ensure that our desire to help does not override a patients' wishes or values. Ethics committees and institutional review boards (IRB) play key roles in the evaluation and approval of clinical investigations and must be heeded. *Arthroscopy* has long required IRB approval of clinical research and more recently called for formal registration of clinical trials as an ideal for publication.

Some argue in favor of "the reverse translation research paradigm," asserting, "It's time to reverse our

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thinking" because "[t]he beauty of reverse translation, unlike benchtop-to-bedside research, is that there is no such thing as a failed clinical trial; only expected and unexpected therapeutic outcomes, and the inevitable variability in the observed human therapeutic response that needs further explanation and exploration."[20] Others argue that translational research, reverse or otherwise, advances knowledge, and both preclinical and clinical research are translational if the goal is to address therapeutic failure.[21]

These arguments seem elegant but rhetorical and, frankly, specious. From our point of view, trials investigating treatments that result in poor outcomes really are clinical failures and advancing the knowledge that treatment risks outweigh benefits is not a clinical research goal. Poor outcomes can occur, but rhetoric should not be an excuse for investigating clinical treatments if there is a concern that preclinical investigation could decrease risk.

Reverse translational research is a part of our armamentarium and should not be summarily discounted. However, if feasible, we encourage and prefer preclinical laboratory and basic science investigation—the forward approach—before novel therapeutic intervention. And, when a reverse translational approach seems safe and warranted, clinical innovators and investigators should adhere to bioethical research principals, including collaboration with ethics committees, IRB approval, trial registration, and informed consent. Under certain circumstances, translational research may be bidirectional.

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