NIH Grants Workshop
Significance, Innovation, and Approach (Scope)

Jeff Siewerdsen, PhD
Professor and Vice-Chair – Biomedical Engineering
Johns Hopkins University
Professor – Imaging Physics, Neurosurgery, and Radiation Physics
The UT MD Anderson Cancer Center
Director – Surgical Data Science Program
Institute for Data Science in Oncology (IDSO)

Support & Disclosures

Research Funding Support
National Institutes of Health
U01 NS-107133 (Image-Guided Neurosurgery)
R01 EB-017226 (Imaging for OR Safety and QA)
R01 CA-127444 (Image-Guided Head & Neck Surgery)
R01 CA-112163 (3D Image Quality)
R21 EB-028330 (Video-Guided Ortho Trauma)
Academic-Industry Collaboration
Medtronic (U01 BRP, 3D Imaging, and LongFilm)
Siemens Healthineers (Ortho Surgery and IR)

Advisory Board and/or Licensing
Elekta Oncology
Siemens Healthineers
Carestream Health
Medtronic
Precision X-Ray Imaging
Izotropic
The Phantom Lab
Review Criteria (RESEARCH Grants)

A good way to pass a test is to know the questions.

Scored Review Criteria

- Significance
- Innovation
- Approach
  Investigator(s)
- Environment

9-Point Rating Scale

<table>
<thead>
<tr>
<th>Overall Impact or Criterion Strength</th>
<th>Score</th>
<th>Descriptor</th>
<th>Strengths</th>
<th>Weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>1</td>
<td>Exceptional</td>
<td>Exceptionally strong</td>
<td>Essentially no weaknesses</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Outstanding</td>
<td>Extremely strong</td>
<td>Negligible weaknesses</td>
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<tr>
<td></td>
<td>3</td>
<td>Excellent</td>
<td>Very strong</td>
<td>Some minor weaknesses</td>
</tr>
<tr>
<td>Medium</td>
<td>4</td>
<td>Very good</td>
<td>Strong</td>
<td>Numerous minor weaknesses</td>
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<tr>
<td></td>
<td>5</td>
<td>Good</td>
<td>**</td>
<td>At least one moderate weakness</td>
</tr>
<tr>
<td>Low</td>
<td>7</td>
<td>Fair</td>
<td>**</td>
<td>At least one major weakness</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>Marginal</td>
<td>A few strengths</td>
<td>A few major weaknesses</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>Poor</td>
<td>Very few strengths</td>
<td>Numerous major weaknesses</td>
</tr>
</tbody>
</table>

Significance

SIGNIFICANCE ➔ is about the PROBLEM.

Does the project address an important problem or a critical barrier to progress in the field?

A. Significance

A.1) Medical Errors and Safety Initiatives: The major impact of medical errors and the need for improved patient safety has come dramatically to light in recent years. The seminal report by the IOM, *To Err is Human*, shocked the medical community in finding that ~5-17% of admissions result in a medical error, with ~50% of those being preventable. More recent data show up to 1/4 of hospital admissions meeting an adverse event. Especially in surgery, the frequency of adverse events is startling, with 40-45% of admissions resulting in an adverse event. Even more disturbing, ~25% of errors lead to major additional intervention (grade llb), ~7% in disability, and ~1-7% in death. Among such adverse events, wrong-site surgery, complications, and retained foreign bodies (RFBs) are the most dramatic, leading to costly litigation, damaging publicity, and increased medical cost. Wrong-site surgery (among the most “never events”) occurs ~1-4.5 times per 1,000 surgeries, or ~40 times per week in the US. Similarly (although difficult to ascertain from self-reported data) RFBs occur in 1 of every 1,000–18,000 surgeries and cost an additional ~$53k per case. Efforts to reduce such errors include the JCAHO universal protocol, preoperative site marking, device counts, root cause analysis, event reporting, checklists, and timeouts. A decade into such efforts, however, the data suggest little or no evidence of real progress, and the need for advances beyond existing paradigms is imminent. The proposed work focuses on orthopaedic or neuro spine surgery, where the incidence of adverse events is high — e.g., 16% – 28% of procedures meeting with an adverse event and 91% in relation to the procedure itself. Such errors include wrong-site (wrong-level) surgery, malplacement of devices (pedicle screw breach), and failure to detect RFBs. For example, approximately 1 in 300 spine surgeries results in delivery at the wrong-level, with ~1M spine procedures / yr and ~200% rate of increase over the last decade. For pediatric spine surgery, although the procedure is commonly performed safely, the rate of malplacement is fairly high, with ~2-16% of screws identified as breach in post-op CT and 1 in ~150 patients requiring revision surgery due to neurological problems from screw malplacement.
**Significance**

**SIGNIFICANCE ➔ is about the PROBLEM.**

Does the project address an important problem or a critical barrier to progress in the field?

If the project is successful, how will this work:
- Improve scientific knowledge, technical capability, and/or clinical practice
- Change the concepts, methods, technologies ... in this field

**A.5) Safer Surgery.** The significance of such capabilities in broad utilization is potentially enormous, with implications beyond the conventional domain of high-precision surgery. A long-term vision includes a shift in underlying motivation for image guidance, from refining the precision of the surgeon to enhancing the safety of the patient. The two are clearly related, but a shift in motivation brings an opportunity to transcend conventional barriers to mainstream use and a shift in the role and cost of intraop imaging. From this perspective, the proposed research is well aligned with a changing, cost-sensitive landscape centered on patient safety and resonates with emerging themes in healthcare beyond conventional paradigms of surgical navigation.

And in the Specific Aims:

Successful completion of these Aims offers advances within and beyond spine surgery, developing methods for low-cost, low-dose intraoperative imaging in a potentially broad spectrum of applications. The advances are motivated not by conventional goals of refinement in surgical precision, but by broader challenges to patient safety, addressing major sources of adverse events in the OR in a manner consistent with natural workflow. The research drives the development of novel registration and reconstruction methods to translational clinical studies using an advanced prototype C-arm as an integrated system for OR QA.

**HISTORICAL notes:**

Once upon a time... “Background & Significance” (part of 25-page proposal)

2009: B&S ➔ Significance (and 12-page proposal)

2016: Introduced the concept of PREMISE...

and now **RIGOR** – the quality of being thorough, exhaustive, or accurate

**The quality / strength of prior work that forms the basis for the proposed research**

**An opportunity to include Preliminary Results?**

Maybe (R01 proposal)

**But do not confuse Significance with Innovation:**

A significant project is not necessarily innovative.
An innovative project is not necessarily significant.
INNOVATION ➔ is about the SOLUTION (and what’s new / different).

Does the application:
- Challenge / **shift current research or clinical practice paradigms**
- Propose a new theoretical concept, approach, instrument, or intervention

Alternatively, does it:
- Refine or improve
- Give a new application of
- Combine existing (…) in a novel way

... the concept, approach, instrument, or intervention

An opportunity to include Preliminary Results? Yes (R01 proposal)

Use effective structure of Sections – for example:
- B.1 Innovation in Deformable Image Registration
- B.2 Innovation in 3D Image Reconstruction
- B.3 Innovation in Clinical Workflow and QA
**Approach**

**APPROACH → is about YOUR PLAN**

Is the overall strategy, methodology, and analysis appropriate to **accomplish the specific aims of the project?**

- Structure the Approach section according to Specific Aims – for example:
  - C.1 (Aim 1) System for Intraoperative Imaging
  - C.2 (Aim 2) System for Deformable Registration
  - C.3 (Aim 3) Clinical Pilot Studies

Does the project **present quantifiable endpoints, benchmarks**? (For early stages) will the strategy _establish feasibility_ suitable to future work?

Does the project manage particularly risky aspects and **address potential problems, alternative strategies**?

→ Include Potential Pitfalls sections.

**C.3.4 Potential Pitfalls and Alternatives.** Alternative registration methods will be investigated as a basis of comparison and to evaluate robustness to CBCT artifacts. For example, MIND-Demons,23,24 leverages a modality-insensitive neighborhood descriptor and diffeomorphic model for brain registration (e.g., LDDMM).24 In addition, advances in deep learning for deformable registration show promising results – e.g., predictive registration neural networks as in Refs.23,24 that learn similarity and transformation with potential advantages over model-based registration.

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**Overall Impact**

**Summary Statement: Overall Impact**

(Before the SS meeting) Assigned reviewers → preliminary Overall Impact score.

(Following SS discussion) Assigned reviewers modify Overall Impact scores.

Other reviewers see these scores and give Overall Impact score.

SRO computes the **Overall Impact score:**

\[
Overall\ Impact = 10 \times \left( \frac{1}{N_{member}} \right) \sum_{i=1}^{N_{member}} Impact_i
\]

Final Overall Impact score on the summary statement:

- **Range:** 10 (high impact) through 90 (low impact)
- **HIGH Impact (1.0 – 3.0)** higher likelihood of award.
- **Not reported for applications that are ND.**

**IMPACT is vital to the success of your grant.**

Incorporate this in your writing. Be explicit.

Be able give a compelling statement of impact. (Practice this – your _elevator pitch._)
Most Common Grant-Writing Mistakes
(source: NIH)

Problems with Specific Aims
- Too ambitious, too much work proposed
  - Unfocused aims, unclear goals
  - Limited aims and uncertain future directions

Problems with Significance
- Not significant (will not advance science or practice)
  - Not exciting, lacks compelling rationale
  - Incremental → Low impact

Problems with Innovation
- Not clearly addressed
  - Incremental → Not new

Problems with Approach
- Level of Detail
  - Too much unnecessary detail (on established methods)
  - Not enough detail (on untested approaches)
- Preliminary Data (R01)
  - Not enough preliminary data to establish feasibility
  - Feasibility of each aim not shown
  - Little or no expertise with approach
- Study Design
  - Lack of appropriate controls
  - Not directly testing hypothesis
  - Correlative or descriptive data
  - Inadequate consideration of power
  - Experiments not directed towards mechanisms
  - Inadequate discussion of alternative models, potential pitfalls


Most Common Grant-Writing Mistakes
Too Ambitious, Too Much Work Proposed

<table>
<thead>
<tr>
<th>R21 NIAMS</th>
<th>R01 NIBIB</th>
<th>R01 NIBIB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measure Tx response (arthritis) using a novel image-based biomarker.</td>
<td>3 Aims, each 2 novel technologies. Application in brain and spine surgery.</td>
<td>Development and translation of existing methods to 2 new applications in neurosurgery.</td>
</tr>
<tr>
<td>Study Design. Outcome Measures</td>
<td>Scope of Work. Application Focus</td>
<td>Mechanism &amp; Institute. Application Focus</td>
</tr>
<tr>
<td>R21 NIAMS</td>
<td>R01 NIBIB</td>
<td>U01 NINDS</td>
</tr>
<tr>
<td>Measure test-retest reproducibility in the proposed image-based biomarker.</td>
<td>3 Aims: 2 novel technologies + clinical study. Application in spine surgery</td>
<td>Emphasis on clinical translation and biomedical research partnership. Application in DBS.</td>
</tr>
</tbody>
</table>

Less is more!