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

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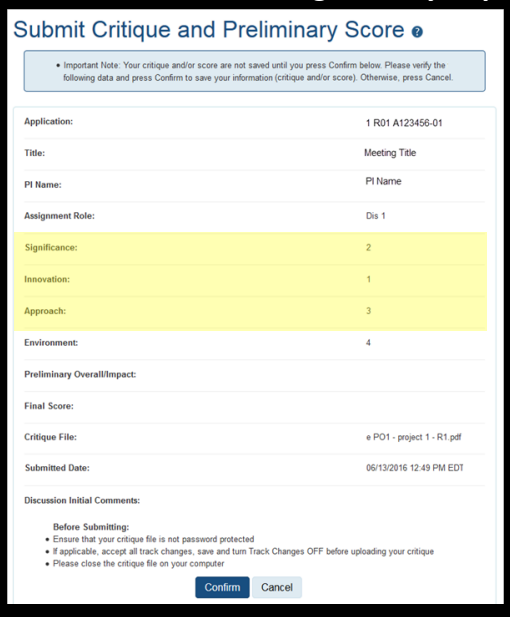
Support & Disclosures

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

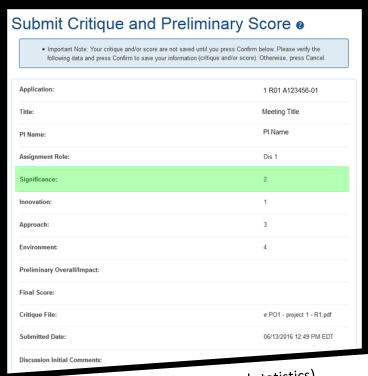
9-Point Rating Scale

Overall Impact or Criterion Strength	Score	Descriptor	Strengths	Weaknesses
High	1	Exceptional	Exceptionally strong	Essentially no weaknesses
	2	Outstanding	Extremely strong	Negligible weaknesses
	3	Excellent	Very strong	Some minor weaknesses
Medium	4	Very good	Strong	Numerous minor weaknesses
	5	Good	" "	At least one moderate weakness
	6	Satisfactory	Some strengths	Some moderate weaknesses
Low	7	Fair	" "	At least one major weakness
	8	Marginal	A few strengths	A few major weaknesses
	9	Poor	Very few strengths	Numerous major weaknesses

Significance

SIGNIFICANCE → is about the PROBLEM.

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



Avoid the perfunctory. (broad, general statistics)
Exciting, specific, and compelling rationale / motivation.

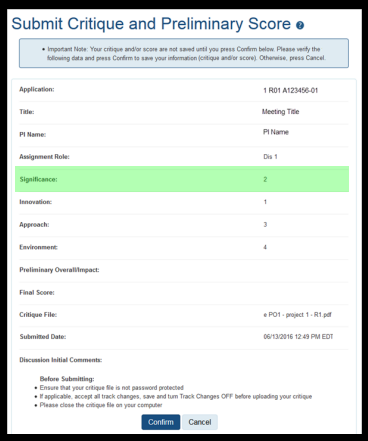
Be quantitative.
Prevalence. Incidence. Cost. Quality-of-life years.

Significance is both **clinical and scientific**.
This section has a strong influence on **IMPACT**.

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.[1] More recent data[3] 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.[4] Even more disturbing, ~25% of errors lead to major additional intervention (grade IIb), ~7% in disability, and ~1-7% in death.[5-11] Among such adverse events, **wrong-site surgery**, **complications**, and **retained foreign bodies (RFBs)** are the most dramatic, leading to costly litigation,[12] damaging publicity, and increased medical cost. Wrong-site surgery (among the foremost "never events") occurs ~1-4.5 times per 1,000 surgeries,[13] or ~40 times per week in the US.[14] Similarly (although difficult to ascertain from self-reported data) RFBs occur in 1 of every 1,000–18,000 surgeries[15-17] and cost an additional ~$53k per case.[18] Efforts to reduce such errors include the JCAHO universal protocol, preoperative site marking, device counts, root cause analysis, event reporting, checklists, and timeouts.[19] A decade into such efforts, however, the data suggest little or no evidence of real progress,[20, 21] 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.[22-27] Such errors include **wrong-site (wrong-level) surgery**, **malplacement of devices (pedicle screw breach), and failure to detect RFBs**. For example, approximately 1 in 3000 spine surgeries results in delivery at the wrong-level[28] (with ~1M spine procedures / yr and a ~200% rate of increase over the last decade).[29-31] Similarly for pedicle screw placement, 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.[2, 32, 33]

Significance


Submit Critique and Preliminary Score

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Application:	1 R01 A123456-01
Title:	Meeting Title
PI Name:	PI Name
Assignment Role:	Dis 1
Significance:	2
Innovation:	1
Approach:	3
Environment:	4
Preliminary Overall/Impact:	
Final Score:	
Critique File:	e PO1 - project 1 - R1.pdf
Submitted Date:	06/13/2016 12:49 PM EDT

Discussion Initial Comments:

Before Submitting:
- Ensure that your critique file is not password protected
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SIGNIFICANCE → is about the PROBLEM.

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

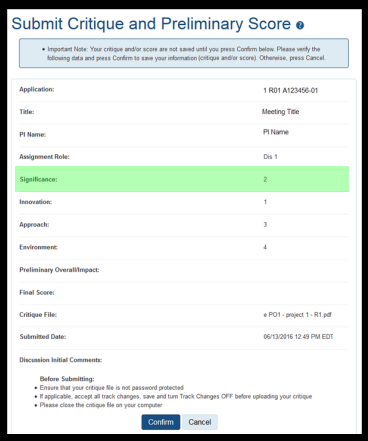
If the project is successful, how will this work:
- Improve **scientific knowledge, technical capability, and/or clinical practice**
- Change the **concepts, methods, technologies** … in this field

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.

Significance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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***

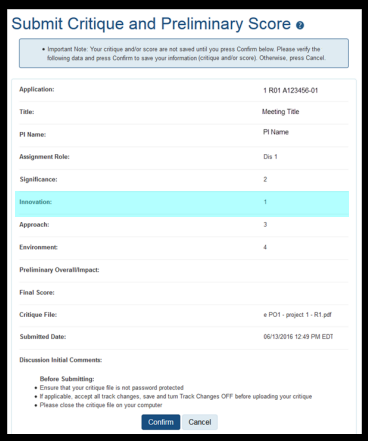
An opportunity to include Preliminary Results?

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



INNOVATION → is about the SOLUTION (and what's new / different).

Does the application:

Challenge / **shift current research or clinical practice paradigms**

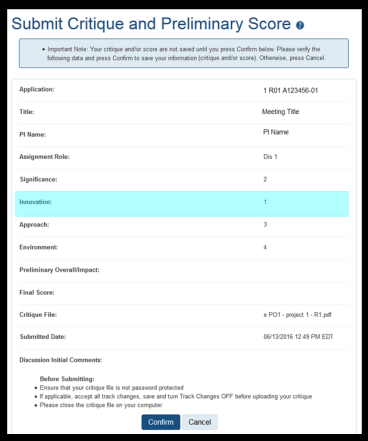
Propose **a new theoretical concept, approach, instrument, or intervention**

Alternatively, does it:

- Refine or improve
- Give a new application of
- Combine existing {…}

… the concept, approach, instrument, or intervention

Innovation



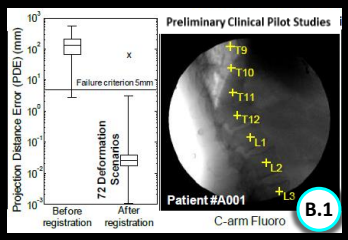
INNOVATION → is about the SOLUTION (and what's new / different).

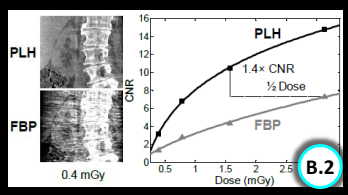
An opportunity to include Preliminary Results?

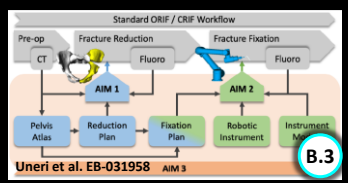
Yes (R01 proposal)

Use effective structure of Sections – for example:

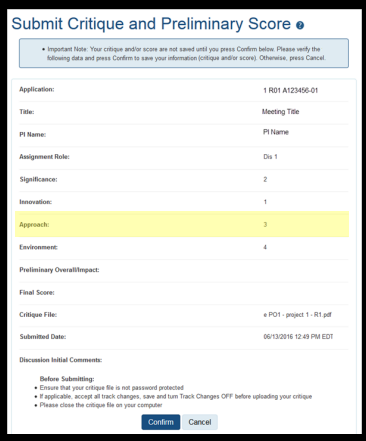
- B.1 Innovation in Deformable Image Registration
- B.2 Innovation in 3D Image Reconstruction
- B.3 Innovation in Clinical Workflow and QA







Approach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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

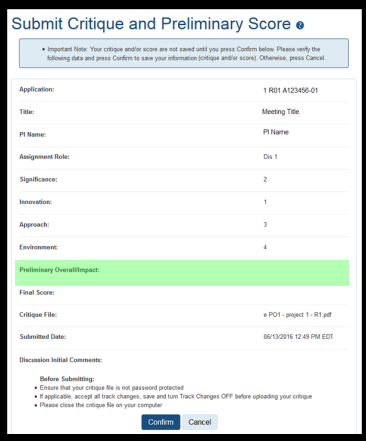
Does the project **present quantifiable endpoints, benchmarks**?
(For early stages) will the strategy **establish feasibility** suitable to future work?

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).[115] In addition, advances in deep learning for deformable registration show promising results – e.g., predictive registration neural networks as in Refs.[116–118] that learn similarity and transformation with potential advantages over model-based registration.

Overall Impact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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.)

9-Point Rating Scale

Overall Impact or Criterion Strength	Score	Descriptor
High	1	Exceptional
	2	Outstanding
	3	Excellent
Medium	4	Very good
	5	Good
	6	Satisfactory
Low	7	Fair
	8	Marginal
	9	Poor

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

https://www.nimh.nih.gov/funding/grant-writing-and-application-process/common-mistakes-in-writing-applications

Most Common Grant-Writing Mistakes

Too Ambitious, Too Much Work Proposed

R21 NIAMS

Measure Tx response (arthritis) using a novel image-based biomarker.

Study Design. Outcome Measures

R21 NIAMS

Measure test-retest reproducibility in the proposed image-based biomarker.

R01 NIBIB

3 Aims, each 2 novel technologies. Application in brain and spine surgery.

Scope of Work. Application Focus

R01 NIBIB

3 Aims: 2 novel technologies + clinical study. Application in spine surgery

R01 NIBIB

Development and translation of existing methods to 2 new applications in neurosurgery.

Mechanism & Institute. Application Focus

U01 NINDS

Emphasis on clinical translation and biomedical research partnership. Application in DBS.