The importance of engineering design constraints to justify a study, particularly in an applied bioengineering journal.

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Editorial

In Journal articles, particularly applied bioengineering journals it is important to put the study in the appropriate context. This is essentially determining the clinical impact. There are multiple ways this can be looked at: the desired clinical performance improvement, the potential effect on clinical performance of a solution, or the benefit (cost, time, resources) to critical stakeholders (patient or health-care providers). The first way is part of the engineering design process. The second is also part of the engineering design process, but is what a research study should show. The third is also part of the engineering design process, but is more a commercializability concern. It is difficult to get funding for or publish articles that are in the final stages of product development, but any paper should be able to place the research in the continuum of steps toward the development of a marketable product.

This is important for justification; justification of the need for the study, the approach used, and the significance of the results. It depends, to a degree on the type of study and where in the design process it fits. An applied paper should be design driven, even if it is written as hypothesis driven. There should therefore be design constraints. The study should explain where it fits in meeting these design constraints. Design constraints can be broken down into different types. There are "have to(s)" and "would like to(s)", which can be clinical performance design constraints as well as pre-clinical design constraints.

Each study should also have its own design constraints; what it is trying to show relative to the design constraint(s) with emphasis on the clinical performance design constraints. Then the significance of the study can be related to meeting the studies design constraints as well as how the limitations of the methodology effect the ability to meet these study design constraints and relate to the clinical performance design constraints.

In order to better understand how design constraints fit in, it would be helpful to explain them in terms of the engineering design process including the commercializability as well as give a practical example. There are a number of places that papers typically fall short related to the engineering design process, which effects its ability to justify the study, the approach, and/or the significance of the study. First is in establishing a problem.

This is in two parts:

1) How far short of the needed clinical parameters are current treatments?

2) How significant a problem is this? In essence a cost/benefit analysis: is the potential benefit of the solution worth the cost and time to develop as well taking into account any associated risks. Part of this is determining how big a difference in clinical performance would actually make a difference (significant clinical impact).

After establishing the problem; the design constraints can be developed. What would success look like? What should the design do as a minimum? Then any proposed solution should be assessed on if it meets all the "have to" design constraints as well as any "would like to" design constraints. The comparison of solutions should be on the clinical significance of meeting each of their "would like to" design constraints as well as their associated costs and risks, since any solution not meeting a "have to" design constraint can be eliminated. Many of the "would like to" design constraints are meeting the "have to' design constraints above the minimal level. Assessing these improvement "would like to" design constraints again requires determining how big an additional difference in clinical performance would actually make a difference as well as how big an improvement on the "have to" design constraint would lead to that level of difference in clinical performance.

Determining and quantifying design constraints is normally an iterative process. The pre-clinical constraints are what we believe the design needs to be or do in order to meet the clinical performance design constraints, which we are most likely not testing, unless this is a clinical study. So the desired pre-clinical performance design constraints cannot actually be determined until the relationship between pre-clinical performance and clinical performance is known. A study may look at just feasibility of meeting the pre-clinical design constraints. It can also look at grouping design constraints (something that could be helpful in simplifying quality control in the future); to build a design constraint hierarchy--either to show that meeting a design constraint is sufficient to meet (predictive of) another design constraint (e.g. an animal model is predictive of clinical performance) higher up in the hierarchy or that meeting a design constraint means that one's below it on the hierarchy have been met.

Although again since it is unlikely that the design process is complete; where the study fits into the process has to be justified. As a minimum the problem and its significance has to be specified. Again, in most cases the complete set of design constraints are not known nor the relationship between pre-clinical design constraints and clinical performance design constraints. As a minimum the specific improvement in clinical performance should be specified (as quantitatively as possible) as well as the believed relationship between the pre-clinical performance design constraint(s) the study is focusing on and the clinical performance design constraints (as quantitatively as possible). Again there are likely multiple relationships to get

from the study focused design constraints to the desired clinical performance.

A study needs to justify where it is in this design process for the specific clinical problem. It is fine, if it is a feasibility study to determine if the proposed solution has the potential to meet the pre-clinical design constraint(s), which could potentially allow it to meet the clinical performance design constraint(s), it just needs to state the purpose of the study. In the discussion, what the study showed relative to the design process should be explained as well as, at least in general, what future studies are needed to determine if the proposed solution could meet the clinical performance design constraints. Too often a paper will claim it showed the potential of the solution to be used in a clinical situation without identifying the problem with current solutions, the improvement in clinical performance desired, or what additional studies would be needed to show the solution could meet the clinical performance design constraints.

Although not typically addressed in applied bioengineering research papers, commercializability is what really determines if the design that meets or exceeds the clinical performance design constraints actually makes it to the market. It is the difference between saying the proposed solution "would make a good clinical product" *vs* "has the potential to meet or exceed the clinical performance design constraints" (solve the problem). It is not necessary to fully discuss the commercializability, but some aspects should be presented, at least in the introduction, to justify the study. Mostly to show the significance of the problem and benefits of coming up with a better solution.

To a large degree assessing the commercializability is looking at the cost *vs* benefits for each stakeholder. Most commercializability concerns can also be considered design constraints. So either look at the value added (benefit) to each stakeholder *vs.* the additional costs to each stakeholder. It can also be looked at as minimum or maximum target values for market size, sales, profit, cost and time of development (including regulatory), patentability, etc.

An example, to illustrate the use of design constraints will be in fracture healing of long bones in professional athletes, which require implanted hardware.

The problem is

(1) The high complication rates.

(2) That the designs interfere with healing; lengthening the rehabilitation time.

Many of the complications (e.g., refracture of the bone) can be reduced by speeding healing. In clinical practice, implants are removed (80% of the time in many cases) to speed healing and reduce long-term complications [1-4]. This typically requires a second rehabilitation cycle and in many cases leaves holes in the bone, which increase the susceptibility to refracture.

The clinical performance goal is to return the athlete to the activity as soon as possible. The clinical performance design constraints could be reducing average healing and recovery time by 50% and the overall cost of treatment by 25%. This can be turned into cost savings per procedure as well as with certain market shares [5].

The strategy employed is to use a degradable metal implant device [6]. It is believed that this solution will meet the clinical performance design constraints by speeding the healing by at least 20% and eliminating the need for a removal surgery (with a second rehabilitation cycle). This will be achieved by having a material comparable to current devices in load carrying ability with stiffness closer to bone, which decreases over time. The bone heals faster with more loads on it (which happens with a less stiff implant) as long as the load to failure of the fracture or implant is not exceeded. The device is to be designed to have a surface layer which stays relatively intact until the fracture is about 90% healed then starts to degrade away. This assures the load on the bone is more than current treatments at any given time point and the failure loads of the fracture or implant are never exceeded [7,8].

Studies are done to determine the degradation of the material in different environments with different surface treatments. Early studies were to show the feasibility of creating a thin surface layer that lasts for at least 3 months and maintains its load to failure and stiffness relatively constant over that time frame. It also moved from initial degradation rate, to *in-vitro* and then *in- vivo* degradation rates. Ultimately the relationship between initial degradation rate and clinical degradation rate needs to be determined (as well as bone healing rate and typical loading levels). Then a clinical study would have to be done to prove that if the clinical degradation rate constraint is met then the clinical performance design constraints will be met [8].

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