SimSight: Data Mining to Determine the Role of Computational Modeling and Simulation in Regulatory Decisions for Marketed Medical Devices

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KEY TAKEAWAYS

- Computational modeling and simulation is used to support marketing applications for a broad range of medical devices.
- There are different modeling disciplines that are accepted (see Figure 3). For example,
  - Solid mechanics (e.g., fatigue assessment)
  - Fluid dynamics (e.g., shear stress calculations)
  - Electromagnetics (e.g., specific absorption rate due to radiofrequency energy)
  - Heat transfer (e.g., tissue damage due to temperature)
- Since 2002, at least 21% of 565 original premarket approval (PMA) applications had computational modeling efforts provided in the Summary of Safety and Effectiveness Data (SSED).

BACKGROUND

The Center for Devices and Radiological Health (CDRH) regulates a broad range of medical devices of different types, and different risk classifications:

- Low risk devices (e.g., tongue depressors)
- Moderate risk devices (e.g., catheters)
- High risk devices (e.g., heart valves)

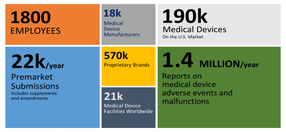


Figure 1: Scope of CDRH regulation.

There are four types of models that are used to support the evaluation of medical devices: animal, bench, computational and clinical. See Figure 2. See Reference [1] for more details

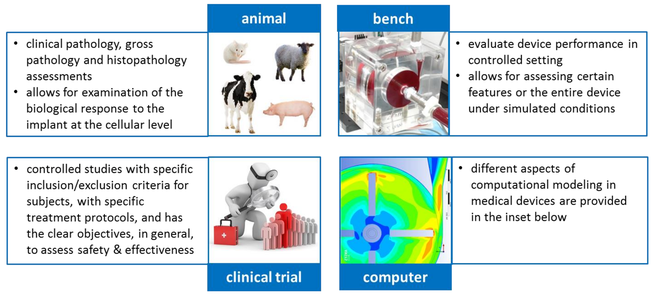


Figure 2: Types of models used to support medical device evaluation.

There are a variety of modeling disciplines such as computational solid mechanics, computational electromagnetics, computational fluid dynamics, and computational thermal analysis. See Figure 3.

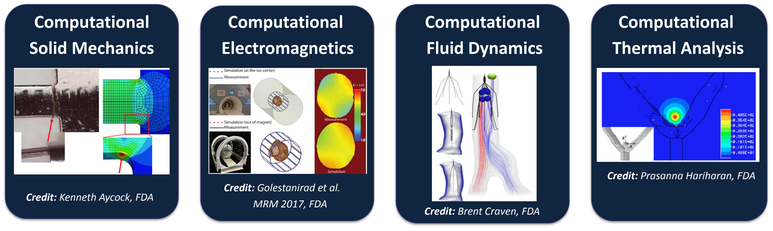


Figure 3: Some of the physics-based modeling disciplines associated with medical devices at the FDA.

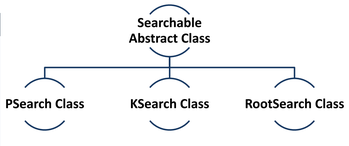
GOAL: To better understand the role and scope of modeling and simulation in the regulatory approval of medical devices, we wanted to determine the number of PMA approvals where modeling and simulation was provided as part of the SSED. We took advantage of FDA data that is publicly available, and as such, the search tools will also be shared with the public. See Reference [2].

METHODS

The methods we employed has three different parts: search tools, search strategy and test strategy.

I. SEARCH TOOL: A Python-based search tool was created that employs an object-oriented approach.* All codes are freely available online at Github.

Searchable	PSearch	KSearch	RootSearch
Root	downloadSums()	downloadSums()	
Index	resultValues()		
fullTextSearch()	compileSpreadsheet()		
printResults()	plotTotal()		
compileResults()			



*Libraries used: Woosh, PyPDF2, Matplotlib, Ipywidgets

II. SEARCH STRATEGY: SimSight was employed to search for modeling and simulation keywords in the SSED of original PMA's approved after 2002. We searched scores of relevant keywords related to modeling and simulation (see below).

- Total Keywords: 97

Approach
I. SimSight: Search all SSED's
II. Sub-search
III. Manual Review

TECHNIQUE		GENERAL		APPLICATION		
finite element	cfd	simulation	computer	mri model	optics model	thermal model
finite element analysis	computational fluid dynamics	simulate	computation	electromagnetic model	optics models	thermal models
fea	computer fluid dynamics	simulating	computational	electromagnetic models	optics modeled	thermal modeling
finite element model	computed fluid dynamics	simulations	computing	electromagnetic modeling	optic model	thermal modeled
finite element modeling	computational fluid dynamic	simulates	compute	electromagnetic modeled	optic models	virtual Population
finite element method	computer fluid dynamic	simulated	computed	computed electromagnetic model	optic modeling	virtualization
finite element models	compute fluid dynamic	quantitative analysis	mathematical model	MRI modeled	modeled	virtualized
finted element modeled	computing fluid dynamic	quantitative model	mathematical modeling	magnetic resonance imaging model	computed optics	virtualizations
finite element analyzed	computation fluid dynamic	quantitative models	mathematical models	magnetic resonance imaging models	computed optic	virtual platform
		quantitative modeling	mathematical modeled	magnetic resonance imaging modeling	computed acoustics	vf
numerical analysis		quantitatively analyzed	math model	magnetic resonance imaging modeled	computed acoustic	virtual patients
numeric analysis		quantitatively modeled	math modeling	thermal modeling	computing acoustics	virtual reality
numerically analyzed		physics modeling	mathematics model	thermal model	computing acoustic	vr
		physics modeled	mathematics models	thermal modeled	acoustic model	software as medical device
		math modeled	mathematics modeling	thermal models	acoustic	
		math models	mathematics modeled			

III. TESTING STRATEGY: SimSight was employed to search for modeling and simulation keywords for any original PMA approved after 2002. In order to ensure that the results retrieved from the search contain the appropriate use and application of the key terms, we employed the following test strategy to check for errors in the software and the results.

Database Access Test
- Database crawl
- PDF to Text
- File storage

Search Test
- PMA files
- Types of Keywords
- Special Characters
- Exact match

Results Compile Test
- File format
- File naming
- Matches captured

RESULTS: I. CODE

Figure 4 below is a schematic of the workflow of the software tool SinSight that we created. The code specifications are provided below the figure.

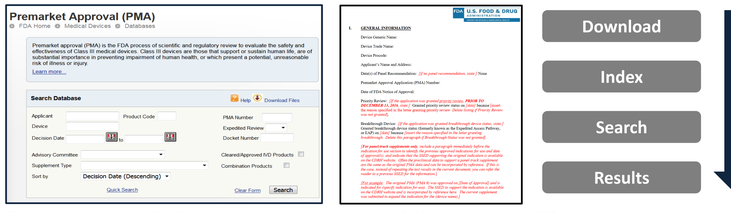


Figure 4: Workflow for the SimSight software tool, which starts with the PMA database, retrieve SSED, index then search for keywords.

Code Runtime Specifications (performed on a laptop)

- 625 lines of code
- 4 publicly available libraries*
- Download (2002-2019): ~ 10 min
- Index: ~ 5 min
- Search: < 1 min
- Compiling Results: < 10^ min

^ Runtime is dependent on keyword

RESULTS: II. SEARCH

Figure 5-7 capture the key results from using the SimSight search tool on the 565 SSED's of approved PMAs since 2002. Note that 34% of approved PMAs come from cardiovascular medical devices.

FIGURE 5: Number of Original PMA SSED's by Year and Advisory Committee

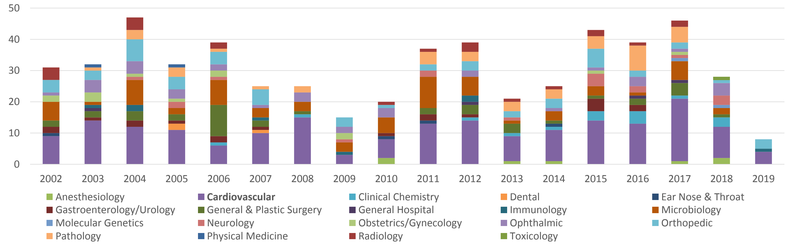
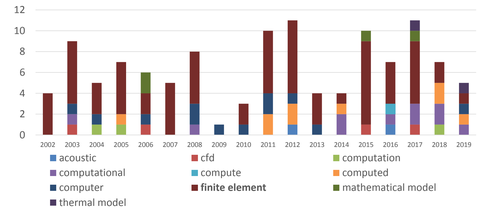


FIGURE 6: Number of Original PMA SSED's with Computational Modeling by Year and Keyword



Total Number of Original PMA SSED's with Computational Modeling by Keyword

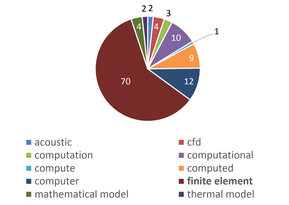
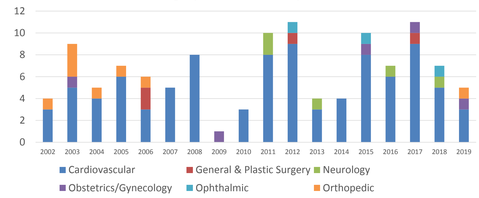
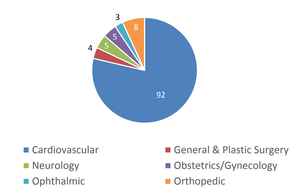


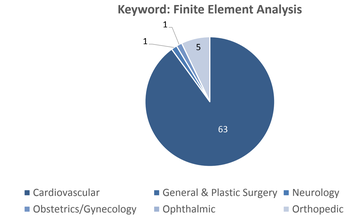
FIGURE 7: Number of Original PMA SSED's with Computational Modeling by Year and Advisory Committee



Total Number of Original PMA SSED's with Computational Modeling by Advisory Committee



Keyword: Finite Element Analysis



Keywords	Matches
finite element	**70**
computer	12
computational	10
computed	9
mathematical model	4
cfd	4
computation	3
acoustic	2
thermal model	2
compute	1

CONCLUSIONS

Computational modeling and simulation are used as supporting evidence in medical device submissions. Of the 565 PMA's approved since 2002, 117 of them included computational modeling as part of the SSED. Finite element analysis is the most prevalent modeling discipline, and is more widely used in the cardiovascular device space. Additional investigations are underway.

This is the first quantitative approach for determining how many submissions have relied on physics-based modeling and simulation for medical devices. With SimSight, we will be able to quantify, track, and later review in more detail, the use of computational modeling and simulation in regulatory reviews and decision-making for medical devices. Lastly, SimSight is customizable to search for *any* keyword, making a potentially useful search tool for reviewers and the public.

LIMITATIONS & FUTURE WORK

One key limitation of the search tool is that we are not able to search original PMA's before 2002. The SSED's available in the public database before 2002 are images and thus currently are not text searchable. Also, because not all PMA supplements result in an SSED, we are not able to search, at this time, for approved panel-track supplements.

Our future work efforts are to refine the keywords (e.g., include (Q)SAR), search the 510(k) database with the same keywords, develop capabilities to convert images to text, and to search approved PMA panel-track supplements. Lastly, we intend to pull the regulatory submissions with computational modeling results and investigate the nature of the computational modeling, what question was being addressed with modeling and determine what role it played in decision-making.

REFERENCES

[1] Morrison, T. M., *et al.*, (2018). Advancing regulatory science with computational modeling for medical devices at the FDA's Office of Science and Engineering Laboratories. *Frontiers in medicine*, *5*.

[2] Kumsa, Doe, et al. "Public regulatory databases as a source of insight for neuromodulation devices stimulation parameters." Neuromodulation: Technology at the Neural Interface 21.2 (2018): 117-125.

DISCLAIMER

SimSight research tool is currently in the testing phase of development and therefore, ***results are considered preliminary***. All data are from the FDA public database; no proprietary information is being shared. Results should not be used for regulatory decision-making purposes.

ACKNOWLEDGEMENTS

Mitchell Fanger is an intern supported by the FDA Pathways Program. He is a rising sophomore at the University of Maryland studying computer engineering.