20184

A Hypothesis-Driven Parametric Study of a Computational Dermal Replacement Model

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ABSTRACT IMPACT: This work will be used to improve the design of engineered dermal replacements that can be used to treat difficult-to-heal wounds such as burns or ulcers. OBJECTIVES/GOALS: Wounds of the skin are among the most common and costly medical problems experienced. Engineered dermal replacements have been developed to improve outcomes, but the optimal design features are unknown. Here we describe a hypothesis-driven study of scaffold parameters using a computational model of wound healing to simulate a variety of treatments. METHODS/STUDY POPULATION: The computational model, which was informed by animal data, was used to simulate cell, cytokine, and collagen density fields. There are reciprocal mechanobiological interactions between the cells and collagen that guide the wound healing process. We analyzed initial wound properties such as scaffold stiffness, microstructure, degradation, and wound geometry by running a one-at-a-time order-of-magnitude parameter change. We then conducted a derivative-based local sensitivity analysis for simulated experimental conditions and constructed a surrogate model of wound contraction using Gaussian process regression. RESULTS/ANTICIPATED RESULTS: We conducted finite element model simulations of scaffolds that varied in physical properties. A sensitivity analysis demonstrated that wound contraction was highly sensitive to collagen fiber stiffness and density. Wound contraction rate was also dependent on initial wound size and surface area. Collagen fiber orientation in the scaffolds affected contraction directionality and the orientation of the final wound area. A Gaussian process regression model was fit to the simulation results for use in rapid prototyping of scaffolds for design optimization. The Gaussian process model was able to reproduce the wound contracture for training and test cases. DISCUSSION/SIGNIFICANCE OF FINDINGS: This work further analyzes a computational model of wounds treated with collagen scaffold dermal replacements. The hypothesis driven analysis of the model suggested several key design features of scaffolds. The model surrogate will further be used for the purposes of prediction and optimization of tissue regeneration outcomes.

Commercialization/Entrepreneurship

26600

HiTech and Health Interest Trends in Rural Neighborhoods are Associated with COVID-19

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ABSTRACT IMPACT: Current, complete, unbiased, and accurate information, which includes patient social and environmental context, is necessary to understand health outcomes. OBJECTIVES/GOALS: Literacy in technology empowers patients in improving their health. We hypothesize that by integrating this information into clinical information, obfuscated relationships may become apparent. To test this, we have combined technological literacy elements with clinical data and test results from patients at risk for severe COVID-19 reactions. METHODS/STUDY POPULATION: Zip level data was appended to approximately 55,000 clinical records of COVID-19 positive and negative patients with comorbidities linked to high illness severity (e.g., diabetes, heart disease). The patient zip code was matched to zip code level health and technology interest indicators. Health interest indicates the level of interest in health such as research, exercising, better dieting, preventive care, etc., and is ranked from 0 to 9. The technology interest indicator is a binary flag indicating technology adopters. These lifestyle factor data points were obtained from survey data and purchasing patterns using transactional and response information from self-reported sources. For each zip code, the index values were represented by a percentage of that population. RESULTS/ANTICIPATED RESULTS: There is a pronounced difference between urban and rural areas with respect to interest in health and technology. In neighborhoods where most residents are interested in both health and technology, the percentage of COVID-19 cases was smaller. A Wilcoxon signed-rank test indicated that the distributions were statistically different (p-value = 4.606e-06) when evaluating the low interest values for health and technology, and (p-value = 1.069e-09) when there was high interest in health and technology against COVID-19 results. In addition, the health and technology indicator variables are not correlated with income at the zip code level. At the low index values, interest in health and technology, the correlation was -0.0856, and at the high end, the correlation was -0.0436. DISCUSSION/SIGNIFICANCE OF FINDINGS: This result is significant for COVID-19 research because it describes a methodology for identifying patients who may be at higher risk for contracting the disease. This relationship was reflected in electronic health record data only after zip-level information was added. Moreover, this was true at across income levels.

Dissemination and Implementation

90552

Evidence synthesis with reconstructed survival data

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ABSTRACT IMPACT: A one-stage Bayesian multilevel model for meta-analysis integrating different survival data is introduced to complete the information synthesis without assuming proportional hazard. OBJECTIVES/GOALS: To develop a general modeling approach to perform efficient and robust meta-analyses using aggregated data (AD) for survival type endpoint and apply to a meta-analysis to examine the association between measurable residual disease (MRD) and disease-free survival (DFS) and overall survival (OS) in patients with acute myeloid leukemia (AML). METHODS/STUDY POPULATION: A Bayesian semi-parametric hierarchical model with a time-varying HR effect was presented. Three common types of survival information, including reconstructed survival data, the hazard ratio (HR) estimates with corresponding CIs and survival rates at specific time points, are synthesized such that all literature from the systematic review can contribute properly to the estimation and uncertainty quantification of the model parameters. The

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time-varying effects was modeled by assuming piecewise hazard risk and piecewise constant hazard ratio. The heterogeneity across studies was expressed by an additive random study effect and a random treatment-by-study interaction. The method was applied to a systematic review of 81 publications reporting on 11,151 AML patients. RESULTS/ANTICIPATED RESULTS: In simulation studies that the proportional hazard assumption is either valid or violated, the proposed method was efficient to achieve comparable performance to IPD meta-analysis, a gold standard approach, in estimating the survival rates, the restricted mean survival time at specific time points and median survival time with the point estimates close to the true values. When HR is not proportional over time, the proposed method was robust in estimating HR and significantly outperformed the classical random-effects meta-analysis. In the application to AML study, the average HR for achieving MRD negativity was 0.36 (95% CrI, 0.33-0.39) for OS and 0.37 (95% CrI, 0.34-0.40) for DFS. The association of MRD negativity with OS and DFS was significant and consistent across all subgroups. DISCUSSION/SIGNIFICANCE OF FINDINGS: The proposed novel method provided a flexible framework for meta-analysis of survival data, to accommodate various types of survival data in one model without assuming proportional hazards assumption. The findings of AML meta-analysis suggest that achievement of MRD negativity is associated with superior DFS and OS in patients with AML.

Education/Mentoring/Professional and Career Development

62859

Bringing Exposures into Mainstream Translational Research: Informatics Opportunities and Methods

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ABSTRACT IMPACT: This work will discuss informatics methods enabling the use of exposure health data in translational research. OBJECTIVES/GOALS: 1. Characterize gaps and formal informatics methods and approaches for enabling use of exposure health in translational research. 2. Education of informatics methods enabling use of exposure health data in translational research. METHODS/STUDY POPULATION: We performed a scoping review of selected literature from PubMed and Scopus. In addition we reviewed literature and documentation of projects using exposure health data in translation research. RESULTS/ANTICIPATED RESULTS: Primary challenges to use of exposure health data in translational research include: (1) Generation of comprehensive spatio-temporal records of exposures, (2) Integration of exposure data with other types of biomedical data, and (3) Uncertainties associated with using data as exact quantifications of exposure which are dependent on both - the proximity of measurement to subject under consideration and the capabilities of measuring devices. We identified 9 major informatics methods that enable incorporation and use of exposure health data in translational research. While there are existing and ongoing efforts in developing informatics methods for ease of incorporating exposure health in translational research, there is a need to further develop formal informatics methods and approaches. DISCUSSION/SIGNIFICANCE OF FINDINGS: Depending on the source about 50 - 75% of our health can be quantified to be a contribution of our environment and lifestyles. In this presentation, we summarize the studies and literature we identified and discuss our key findings and gaps in informatics methods and conclude by discussing how we are covering these topics in an informatics courses.

70329

Automated Lungs Segmentation and Airways Skeletonization from CT Scans in Patients with Cystic Fibrosis

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ABSTRACT IMPACT: Improve healthcare of patients with Cystic Fibrosis by reducing the time needed to generate results. OBJECTIVES/GOALS: We developed an automated framework capable of segmenting the lungs, extract the airways, and create a skeletonize map of the airways from CT scans of Cystic Fibrosis patients. As future expansion, the framework will be expanded to measure the airways diameters, detect the abnormal airways, and count the number of visible airways generations. METHODS/STUDY POPULATION: For this study, 35 CT scans from CF patients with different levels of severity were used to test the developed framework. The lungs segmentation was performed using an algorithm based on Gaussian Mixture Models for mild cases, and for severe cases a technique that uses convex hull and the recurrent addition of 'dots' was implemented. The airways extraction was performed using a 26-points connected components algorithm in conjunction with a curve fitting technique over the histogram of voxel values. Medial axis transform was used to perform the skeletonization of the extracted airways, and airways diameters determined via ray-casting. RESULTS/ANTICIPATED RESULTS: The framework was able to correctly obtain the segmented lungs in all 35 sample volumes regardless of disease severity. In contrast, it tends to fail to skeletonize the airways for severe cases where the framework is unable to differentiate between abnormal lungs conditions and dilated airways. Fine tuning is required to achieve better results. The expected result of the future implemented sections of the framework are focused to characterize the extracted airways by: 1) measuring the airways diameters; 2) detect and count the number of abnormal airways sizes; and 3) count the number of visible airways branching which will permit determination of stage and grade of the lungs of CF patients. DISCUSSION/SIGNIFICANCE OF FINDINGS: The proposed framework allows a fast and reproducible way to segment the lungs and create a skeletonized map of the airways that are independent of clinical training. In addition, this framework will be extended to obtain measurements of airway dilation and branching level, which could provide a deeper insight of the airways in CF patients.

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