## BIOGRAPHICAL SKETCH

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NAME: Márcio Augusto Diniz

eRA COMMONS USER NAME (credential, e.g., agency login): MDINIZ

POSITION TITLE: Research Scientist

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| University of Campinas, São Paulo, Brazil | B.S. | 12/2008 | Statistics |
| University of Campinas, São Paulo, Brazil | M.S. | 02/2011 | Statistics |
| University of São Paulo, São Paulo, Brazil | Ph.D. | 06/2015 | Statistics |

### A. Personal Statement

My areas of expertise relevant to this project are experimental design, biostatistics and bioinformatics. Specifically, I will: (1) Coordinate statistical activities to ensure that investigators have ready access to statistical consultation and support, (2) provide statistical expertise in the design of experiments and studies, including research proposal development, sample size determination, and plans for interim reviews and final analysis, (3) assist with the writing of statistical components of manuscripts, (4) review the integrity and statistical soundness of all studies, (5) provide statistical analysis for all projects using appropriate statistical and computing methodologies, and (6) assist in the interpretation and presentation of results.

### B. Positions and Honors

2012 – 2015 Biostatistician, Department of Gastroenterology, School of Medicine, University of São Paulo, São Paulo, Brazil
2015 – 2020 Research Scientist I, Biostatistics Core, Samuel Oschin Comprehensive Cancer Institute, Cedars Sinai Medical Center, Los Angeles, CA
2017 – Present Assistant Professor, Department of Medicine, Cedars Sinai Medical Center, Los Angeles, CA
2020 – Present Research Scientist II, Biostatistics Core, Samuel Oschin Comprehensive Cancer Institute, Cedars Sinai Medical Center, Los Angeles, CA

### Other Experience and Professional Memberships

2012 – Member, Brazilian Statistical Association (ABE)
2015 – Member, American Statistical Association (ASA)

### C. Contributions to Science

### Bayesian Non-parametric Inference

My early research consisted of developing statistical methodology for estimation of benchmark doses with quantal-response under a Bayesian semi-parametric approach, including previous approaches as special cases.


1. **Diniz MA**, de Bragança Pereira CA, Polpo A. Bayesian Semiparametric Symmetric Models for Binary Data. In Interdisciplinary Bayesian Statistics 2015 (pp. 323-335). Springer International Publishing.

**Phase I Clinical Trials**
My current research consists of developing dose-finding designs applied to single and combination of drugs. In the first article, I extended Continual Reassessment Method (CRM) to incorporate continuous doses and compared it to Escalation with Overdose Control (EWOC); In the second article, I proposed a design taking into account heterogeneity between two complete ordered groups of patients. In the third article, I quantified the loss of information when discrete doses are used instead of continuous dose in model-based designs. Furthermore, I created a R-package to facilitate the implementation of designs proposed by our group.

1. **Diniz MA**, Li Q, Tighiouart M. Dose Finding for Drug Combination in Early Cancer Phase I Trials using Conditional Continual Reassessment Method. Journal of biometrics & biostatistics. 2017;8(6). PMCID: PMC5851015
2. **Diniz MA**, Kim S, Tighiouart M. A Bayesian adaptive design in cancer phase I trials using dose combinations in the presence of a baseline covariate. Journal of Probability and Statistics. 2018. PMCID: PMC6428433
3. **Diniz MA**, Tighiouart M, Rogatko A. Comparison between continuous and discrete doses for model based designs in cancer dose finding. PloS one. 2019 Jan 9;14(1). PMCID: PMC6326565
4. **Diniz MA**. EWOC: Escalation With Overdose Control. R package, version 0.2.0. Available at https://cran.r-project.org/web/packages/ewoc/index.html

**Statistical Analysis of Clinical Data**
My collaborative research with clinicians consisted of analyzing data from observational studies and clinical trials. The following selection are some highlighted peer-reviewed articles: The first article showed that a coordinated, interdisciplinary team caring for SNF patients can reduce 30-day hospital readmissions. The second one demonstrated that High signal on T1-weighted images, grade 2 contrast enhancement, and type 2 enhancement pattern are associated with cerebrovascular ischemic events, which may provide valuable insights into risk stratification. The third article suggested predictive models for bacterial infections and mortality in an emergency department setting. The fourth one conclude that six months of therapy with β-blocker did not ameliorate heart function and morphology in patients with cirrhotic cardiomyopathy.

1. Rosen BT, Halbert RJ, Hart K, **Diniz MA**, Isonaka S, Black JT. The Enhanced Care Program: Impact of a Care Transition Program on 30-Day Hospital Readmissions for Patients Discharged From an Acute Care Facility to Skilled Nursing Facilities. Journal of hospital medicine. 2017 Oct;13(4):229-36. PMID: 29069115
2. Wu F, Ma Q, Song H, Guo X, **Diniz MA**, Song SS, Gonzalez NR, Bi X, Ji X, Li D, Yang Q. Differential Features of Culprit Intracranial Atherosclerotic Lesions: A Whole-Brain Vessel Wall Imaging Study in Patients With Acute Ischemic Stroke. Journal of the American Heart Association. 2018 Aug 7;7(15): e009705. PMCID: PMC6201468
3. Ximenes RO, Farias AQ, Neto AS, **Diniz MA**, Kubota GT, Ivo MM, Colacique CG, D'Albuquerque LA, Dias RD. Patients with cirrhosis in the ED: early predictors of infection and mortality. The American Journal of Emergency Medicine. 2016 Jan 31;34(1):25-9. PMID: 26423777
4. Silvestre OM, Farias AQ, Ramos DS, Furtado MS, Rodrigues AC, Ximenes RO, de Campos M, Daniel F, Yoshimura Zitelli PM, **Diniz MA**, Andrade JL. β-Blocker therapy for cirrhotic cardiomyopathy: a randomized-controlled trial. European journal of gastroenterology & hepatology. 2018 Aug 1;30(8):930-7. PMID: 29979644

**Statistical Analysis of Basic Science Data**
My collaborative research with basic science researchers consisted of analyzing data from mice experiments and elaborate innovative designs. The following selection are some highlighted peer-reviewed articles: The first article demonstrated that anatomic dead space ventilation increases significantly over time in mice in response to mechanical ventilation. The novel functional lung-imaging techniques applied yield sensitive measures of airway volumes that have wide applications. The second one showed that HER3-targenting vaccines activate HER3-specific T cells and induce nti-HER3 specific antibodies, which alters the intratumoral T cell infiltrate and

responses to immune checkpoint inhibition. The third article concluded that in addition to the T cell anti-tumor response induced by Ad-HER3, the HER3-VIAs provide additional functions to eliminate tumors in which HER3 signaling mediates aggressive behavior or acquired resistance to HER2-targeted therapy.


1. Kim EH, Preissner M, Carnibella RP, Samarage CR, Bennett E, **Diniz MA**, Fouras A, Zosky GR, Jones HD. Novel analysis of 4DCT imaging quantifies progressive increases in anatomic dead space during mechanical ventilation in mice. Journal of Applied Physiology. 2017 Jun 8;123(3):578-84. PMCID: PMC5625073
2. Osada T, Morse MA, Hobeika A, **Diniz MA**, Gwin WR, Hartman Z, Wei J, Guo H, Yang XY, Liu CX, Kaneko K. Vaccination targeting human HER3 alters the phenotype of infiltrating T cells and responses to immune checkpoint inhibition. OncoImmunology. 2017 Jun 18:e1315495. PMCID: PMC5486174
3. Osada T, Hartman ZC, Wei J, Lei G, Hobeika AC, Gwin WR, **Diniz MA**, Spector N, Clay TM, Chen W, Morse MA. Polyfunctional anti-human epidermal growth factor receptor 3 (anti-HER3) antibodies induced by HER3 vaccines have multiple mechanisms of antitumor activity against therapy resistant and triple negative breast cancers. Breast Cancer Research. 2018 Aug;20(1):90. PMCID: PMC6085609
4. Kaneko K, Osada T, Morse MA, Gwin WR, Ginzel JD, Snyder JC, Yang XY, Liu CX, **Diniz MA**, Bodoor K, Hughes PF. Heat shock protein 90-targeted photodynamic therapy enables treatment of subcutaneous and visceral tumors. Communications biology. 2020 May 8;3(1):1-4.


Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1B5gSRiar9r58/bibliography/50345686/public/?sort=date&direction=ascending.

**D. Additional Information: Research Support and/or Scholastic Performance**

Ongoing Research Support

P01 CA098912-11 (Chung) 12/01/2002-02/29/2021 0.96 calendar
NIH/NCI
Prostate Cancer Bone Metastasis: Biology and Targeting
Goal: This program project grant focuses on the elucidation of the biology and molecular pathways involved in the interaction between stromal cells of the bone or the prostate and malignant prostate cancer cells.
Role: Biostatistician

NIH UL1 TR001881-01 (Dubinett) 07/01/2016-05/31/2021 0.30 calendar
UCLA Clinical and Translational Science Institute
Support and encourage clinical and translational investigation at Cedars-Sinai Medical Center, UCLA, Harbor-UCLA Medical Center, Drew University, and within the communities these institutions serve.
Role: Biostatistician

SMPAI-2017C2-7716 (IsHak) 07/01/2018-06/30/2021 1.44 calendar
Patient Centered Outcome Research Institute (PCORI)
Personalized Treatments for Depressive Symptoms in Advanced Heart Failure
Goal: It is to generate scientific evidence to help patients, caregivers, and providers, make decisions about how best to manage depressive symptoms in advanced heart failure.
Role: Co-Investigator

U01 CA232859-01 (Rogatko and Gantz) 09/19/2018-08/31/2023 2.40 calendar
NIH/NCI
Advancing Analysis and Interpretation of Adverse Events and PROs in Cancer Clinical Trials
Goal: Apply and extend the Toxicity Index previously proposed by us and other methods to describe toxicity and develop models to determine risk factors for adverse events; and to develop predictive models for limiting dose toxicity, treatment completion, and efficacy based on individual patient characteristics and toxicity profiles defined by the toxicity index and new toxicity summaries from patient reported outcomes.
Role: Co-Investigator

R01 HL147355 (Fan) 04/01/2019-03/31/2024 0.48 calendar
NIH/NHLBI
Longitudinal and quantitative MR plaque imaging for prediction of response to medical management in symptomatic intracranial atherosclerosis
Goal: It is to develop a magnetic resonance technique for prediction of treatment response, which may potentially help prevent recurrent stroke by early identifying non-responsive patients and initiating an alternative therapy.
Role: Biostatistician

U24 NS113452 (Lyden) 08/01/2019-07/28/2022 0.60 calendar
NIH/NINDS
The NIH SPAN Coordinating Center
Goal: The aim of this project is to create a novel system to support parallel testing of promising interventions that—when used in combination with reperfusion—might extend the treatment time window and/or improve outcome after stroke. The SPAN effort affords the highly significant opportunity to find a promising candidate treatment, test it in StrokeNet, and then back-validate the ideal preclinical testing paradigm that predicts success in clinical trials.
Role: Biostatistician

R34 DA050255 (Gao) 09/30/2019-03/29/2021 0.36 calendar
NIH
Planning Phase for the Healthy Brain and child Development Study In Los Angeles County Area
Goal: We aim to establish the feasibility for the large-scale Phase II HEALthy BCD study in the Los Angeles.
Role: Co-Investigator

Thermo Fisher Scientific (Thadhani) 11/23/2019-11/23/2020 0.60 calendar
Internal Grant
Goal: The goal of this study is to identify and validate a cut-off of the sFlt-1/PlGF ratio that can be used to rule-in the risk of developing PE with severe features (as defined by ACOG Guidelines) over a 2 week period in women who are hospitalized with (or develop while hospitalized) a hypertensive disorder of pregnancy.
Role: Biostatistician

W81XWH1910888 (Pandol) 09/30/2019-09/29/2023 0.60 calendar
DoD
Mechanisms and Treatment Development for Pancreatitis Resulting from Alcohol Abuse and Smoking
Goal: This is a Focused Program involving 4 separate but interacting projects with both clinical and pre-clinical models designed to validate mechanisms of smoking and alcohol induced pancreatic disease in humans.
Role: Biostatistician

W81XWH-18-PCRP-HDRA (Vidal) 09/01/2019-08/31/2021 0.24 calendar
DoD
Do Black Men with Metastatic Castration-Resistant Prostate Cancer Have Worse Outcomes than White Patients? A Nationwide VA Study
Goal: The aim of this study is to determine whether long-term outcomes among metastatic castration-resistant prostate cancer patients differ by race.
Role: Biostatistician

ZZ Biotech (Lyden) 12/01/2020 - 11/30/2025 0.60 calendar
Internal Grant
RHAPSODY-2
Goal: A multicenter, randomized, placebo-controlled, double-blinded, Phase 3 study to evaluate the efficacy and safety of 3K3A-APC, a recombinant variant of human activated protein C, in combination with tissue plasminogen activator, mechanical thrombectomy, or both in subjects with moderate to severe acute ischemic stroke: RHAPSODY-2. We seek to establish a safe, effective dose of 3K3A-APC and proceed to a definitive efficacy trial to determine whether 3K3A-APC improves 3-month outcome after stroke and reduces early bleeding associated with recanalization.

Role: Co-Investigator

2R01HL089765-10 (Slomka) 06/01/2020 – 05/31/2024 0.60 calendar
NIH/NHLBI
Quantitative Prediction of Disease and Outcomes from Next Generation SPECT and CT
Goal: The overall aim is to optimize the clinical capabilities of MPS in risk prediction and treatment guidance by integrating all available imaging and clinical data with state-of-the-art AI methods.
Role: Co-Investigator

1R01HL148787-01A1 (Dey) 05/15/2020 – 03/31/2024 0.60 calendar
NIH/NHLBI
Integrated Prediction of Cardiovascular events by automated coronary plaque and pericoronary adipose tissue quantification from CT Angiography
Goal: This new research will allow physicians to more precisely identify patients for whom appropriate treatment could be prescribed, to reduce their risk of future adverse cardiovascular events.
Role: Biostatistician

<u>Completed Research Support</u>

W81XWH-12-1-0447 (Lyerly) 09/30/2012 - 09/29/2017 6.00 calendar
Department of Defense/Duke University
Detecting and Elimination of Oncogenic Signaling Networks in Pre-Malignant & Malignant Cells with Magnetic-Resonance Imagining
Goal: The overall goal of this research is to determine whether novel pre-malignant small molecule inhibitors targeting the intracellular signaling nodes in breast cancer can be utilized for the early detection and characterization using molecular MRI and subsequent RF mediated thermal therapy of malignant cells in vivo.
Role: Biostatistician

206754 (Parker) 02/01/2019-01/31/2020 0.60 calendar
Cedars Sinai Precision Medicine
A Retrospective Pilot Study of the Utility of Circulating Biomarker Panels to Improve Selection of Candidates for Non-Invasive Coronary Artery Calcium Imaging
Goal: The goal of this proposal is to quantify the informativeness of a selective panel of circulating protein biomarkers to identify individuals with measurable CAC-involvement upon subsequent non-invasive imaging for ‘pre-clinical’ atherosclerotic disease
Role: Biostatistician