Dose Savings in Digital Breast Tomosynthesis through Image Processing

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***Abstract*—In x-ray imaging, the ALARA principle defines that the x-ray radiation must be kept as low as reasonably achievable to ensure the patient's safety. However, low-dose acquisitions yield images with low quality, which affect the radiologists' image interpretation. Therefore, there is a compromise between image quality and radiation dose. This work proposes an image restoration framework capable of restoring low-dose acquisitions to achieve the quality of full-dose acquisitions. The contribution of the new method includes the capability of restoring images with quantum and electronic noise, pixel offset and variable detector gain. To validate the image processing chain, a simulation algorithm was proposed. The simulation generates low-dose digital breast tomosynthesis (DBT) projections, starting from full-dose images. To investigate the feasibility of reducing the radiation dose in breast cancer screening programs, a simulated pre-clinical trial was conducted using the simulation and the image processing pipeline proposed in this work. Objective and subjective results suggest that reduction of 30% - 50% in radiation dose could be achieved after the proposed image processing pipeline was applied. Thus, the image processing algorithm has the potential to decrease radiation levels in DBT, also decreasing the cancer induction risks associated with the exam.**

I. Introduction

Breast cancer is the most lethal cancer among women. According to statistics from the Brazilian National Institute of Cancer [1], 57,960 women were diagnosed with breast cancer in Brazil in 2016, and approximately 14,206 deaths were caused by the disease.

The development of breast cancer is relatively rare before the age of 35, and the chances of incidence raise progressively with age, especially in patients older than 50 years. Because the early detection of the disease increases the chances of survival up to 30% [2], many countries adopt breast cancer screening programs. The Brazilian Institute of Cancer recommends that women older than 50 years periodically undergo an imaging exam to detect signs of development of tumors.

For many years, the gold standard imaging modality for breast cancer screening was digital mammography (DM). In DM exams, the breast is exposed to a small dose of x-ray radiation, and a conventional 2-D radiography of the breast is generated. The image is then analyzed by a radiologist, who searches for lesions such as masses, architectural distortions and microcalcifications, which may indicate the development of cancer.

Ph.D. dissertation defended 14^{th} of July 2017

In DM exams, the three-dimensional volume of the breast is projected into a two-dimensional plane. As a result, tissues and structures within the breast may overlap and obscure lesions, decreasing the sensitivity and specificity of the exam [3]. The current sensitivity achieved by DM exams is around 80% [4].

Limitations related to tissue overlap are being solved with the clinical use of digital breast tomosynthesis (DBT) systems. In DBT, 2-D projections are acquired along an arc around the breast. The projections are then reconstructed into tomographic slices, similarly to Computed Tomography (CT) systems. The slices allow the 3-D visualization of the tissues and structures within the breast. Recent studies have shown that the benefits of using DBT for screening purposes include increase on the specificity and sensitivity of cancer detection [5]–[7]

Although DBT is still being developed, it is rapidly becoming a major clinical tool for breast cancer screening. It is known that the performance of radiologists is affected by the quality of the image [8]–[10]. Images acquired with higher radiation dose yield lower relative noise and therefore have better signal-to-noise ratio. However, excessive radiation can represent risks to the patients' health. The literature have shown the risks of cancer induction in healthy women due to the exposure to ionizing radiation during breast cancer screening [11], [12]. Thus, the optimization of radiation dose versus image quality is of great interest in the medical field, especially in screening programs.

A number of works have been proposed to achieve low radiation dose and maintain acceptable image quality. Dose reduction can be achieved, *e.g.*, by the optimization of imaging protocols [13], [14], the improvement of reconstruction algorithms [15], [16], or by applying image restoration algorithms to images acquired at low-dose range [17], [18]. Although many studies have investigated dose savings in conventional imaging modalities, such as CT, the availability of studies about dose savings in DBT is still very limited.

In this work we investigate the feasibility of reducing the radiation dose in DBT exams by restoring images acquired with low-dose. A few other works have been proposed to restore DBT images through denoising [19]–[21]. However, one common issue of these methods is the incompleteness of the noise model assumed, and the smooth appearance observed in the denoised images. We propose a restoration framework dedicated to DBT systems that considers particularities of this imaging modality, and avoids excessive smoothness by the injection of denoised signal into the scaled noisy signal.

To validate studies about dose reduction, such as the one proposed in this work, it would be desirable to have sets of images from the same patient acquired at different radiation levels. However, acquiring such dataset would require repeated exposures of each individual, resulting in risks to the patient's health. To overcome this issue, one common approach is to simulate reduced dose images starting with a standard-dose clinical image.

The development and application of simulation methods for standard imaging modalities such as CT and DM has been widely explored in the literature [22]–[28]. However, to the best of our knowledge, no methods have been proposed or validated on DBT images up to this point.

The task of simulating dose reduction in x-ray images can be divided into two steps: signal scaling and noise insertion. The first step, signal scaling, is straightforward and depends on the linearity of the system being simulated. Generally, x-ray detectors do not present an exact linear response to x-rays, however it is possible to perform mathematical operations to linearize the response.

The second step, noise injection, must be performed with special attention. In digital mammography images, for example, quantum noise is predominant. The quantum noise follows the Poisson distribution, and therefore it has the variance described as a function of the underlying true signal. In clinical applications, the true signal is unknown and therefore the simulation of quantum noise requires some initial assumptions.

The literature presents a number of works that overcome this issue by assuming that the clinical image, acquired with a standard radiation dose, is a good approximation of the underlying signal [23], [24], [26]–[28]. This assumption converges asymptotically as the expectation of the signal increases, as shown in [29], thus an error is associated with this assumption at low photon fluence applications.

Thus, before the restoration method could be validated, we proposed an alternative algorithm for injection of quantum noise into clinical images, to simulate dose reduction. The method performs noise injection in a variance-stabilizing range, and therefore does not require any previous knowledge of the signal. To validate this concept, initial tests were performed on DM images, assuming a simple model of pure white quantum noise. The description and validation of this method was presented in the first work published during this Ph.D. project [30]. The work also presents a complete review of the simulation methods presented in the literature.

As our main goal is to investigate dose reduction in DBT images, in the second part of this work we evaluated our previously presented method applied to DBT images. Because of the lower radiation doses used to acquire each DBT projection, the assumption of pure quantum noise is no longer valid and the electronic noise generated by the detector must be accounted for. Thus, the approximation of a pure quantum noise model resulted in simulation errors, which were published in our second paper [31].

To account for the imaging modalities with lower energies, our noise injection operator was optimized for low photon fluence applications and the new operator was presented in the third published paper [29]. Finally, the operator was modified to adopt a Poisson-Gaussian model, rather than a pure Poisson. The updated model accounts for both quantum and electronic noise. The operator was also modified to account for pixel cross-talk, which causes the noise to be frequency-dependent (non-white). Our fouth published paper [32] describes the complete operator, and the validation on DBT images using objective metrics and a human observer experiment.

After we developed the tool capable of accurately simulating dose reduction in DBT images, we have proposed an image denoising pipeline. In this pipeline, noise suppression was performed on raw DBT projections. The efficiency of the denoising algorithm was improved by choosing a noise model that faithfully represents what is found in DBT images. A Gaussian-Poisson model was chosen, and features such as spatially varying quantum gain, and detector offset were considered in our model. The denoising pipeline was presented and validated on our fifth published paper [33].

In [33], the goal of the proposed denoising pipeline is to enhance, as much as possible, the signal-to-noise ratio (SNR), starting with low-dose DBT images at low SNR ranges. Although the pipeline yields images with high SNR and very low noise, the smooth appearance of denoised images is not appreciated by radiologists.

Thus, the next step of our work was to propose an image restoration framework that uses the denoising pipeline presented previously and controls the image smoothness and SNR by the injection of noisy signal into a denoised signal. The method was formalized and presented in papers [34], [35].

The latest papers [34], [35] presents the final experiments of the Ph.D. thesis. Using objective quality metrics and a two-alternative forced-choice (2-AFC) human observer study we analyzed the performance of our pipeline in terms of mathematical measurements and human perception.

The results presented by the Ph.D. thesis are preliminary to a much greater study that would lead to dose savings in breast cancer screening. Further studies are necessary before the implementation of the proposed method into clinical practice.

A. *Thesis Organization*

The Ph.D. thesis was organized into eight chapters. The first chapter introduced the problems addressed by the work, and provided an overview of the solutions proposed. Chapter 2 presented specific information about the work and explained how each portion of the work is connected to the main objective.

Chapters three to eight presented a series of relevant papers either published or submitted during the development of this project. The papers explain in details the methodology, materials and validation used on each portion of the work. The papers are:

- Borges, L.R.; Oliveira, H.C.; Nunes, P.F.; Bakic, P.R.; Maidment, A.D.A.; Vieira, M.A.C. Method for simulat-

ing dose reduction in digital mammography using the Anscombe transformation. *Medical Physics*, v. 43, n. 6, p. 2704-2714, 2016.
- Borges, L.R.; Guerrero, I.; Bakic, P.R.; Maidment, A.D.A.; Schiabel, H.; Vieira, M.A.C. Simulation of dose reduction in digital breast tomosynthesis. In: *International Workshop on Digital Mammography*, Springer International Publishing, p. 343-350, 2016.
- Borges, L.R.; Vieira, M.A.C.; Foi, A. Unbiased injection of signal-dependent noise in variance-stabilized range. *IEEE Signal Processing Letters*, v. 23, n. 10, p. 1994-1998, 2016.
- Borges, L.R.; Guerrero, I.; Bakic, P.R.; Foi, A.; Maidment, A.D.A.; Vieira, M.A.C. Method for simulating dose reduction in digital breast tomosynthesis. *IEEE Transactions on Medical Imaging*, v. 36, n. 11, p. 2331-2342, 2017.
- Borges, L.R.; Bakic, P.R.; Foi, A.; Maidment, A.D.A.; Vieira, M.A.C. Pipeline for effective denoising of digital mammography and digital breast tomosynthesis. *Proceedings SPIE 10132*, Medical Imaging 2017: Physics of Medical Imaging, 1013206, 2017.
- Borges, L.R.; Azzari, L.; Bakic, P.R.; Maidment, A.D.A.; Vieira, M.A.C.; Foi, A. Restoration of low-dose digital breast tomosynthesis. *Measurement Science and Technology*, v. 29, n. 6, p. 064003, 2018.
- Borges, L.R.; Bakic, P.R.; Maidment, A.D.A.; Vieira, M.A.C. Restored low-dose digital breast tomosynthesis: a perception study. *Proceedings SPIE 10577*, Medical Imaging 2018: Image Perceptiom, Observer Performance, and Technology Assessment, 1057705, 2018.

Note that the two last papers [34], [35] are shown as a single submission in the original thesis. Here we show the final situation of the submission, which was partly published at the 2018 SPIE conference, then extended and submitted to Measurement Science and Technology journal. The final chapter of the thesis presented the general conclusions of the work.

II. Methods

The overall study performed in the thesis is presented in Figure 1 in the form of a flowchart.

The initial portion of the Ph.D. project aimed at developing algorithms to simulate dose reduction in x-ray images, followed by the clinical application of the method to validate image processing methods.

The first two noise-injection operators developed in the thesis adopted a pure Poisson noise model. This model describes the uncertainties predominantly found in applications such as microscopy, many of the x-ray systems, photon-counting systems, etc.

In a Poisson model, the noise variance is a function of the underlying true signal - and therefore is classified as signal-dependent noise. This poses a challenge to the simulation of these variables in real applications. In real systems the underlying true signal is not available and therefore an error is associated to the simulation of extra noise.

The proposed method leverages the properties of variance stabilizing transformations (VST) to perform accurate injection of extra signal-dependent noise into Poisson variables. In the variance stabilizing range, the signal-dependency is ceased. In this scenario, the extra injected noise is independent of the underlying signal, and the noise injection process becomes simple and accurate.

The first operator was based on the Anscombe Transformation, a VST for Poisson variables. The validation was performed on digital mammography images (DM). Due to the high photon fluence found in DM images, the noise can be modeled as Poisson with no harm to the accuracy. This portion of the work are summarized in [30]. The article was published by the *Medical Physics* journal, which has high international relevance (Impact Factor: 2.635), and is classified as A1 by the CAPES Qualis rank. The work was selected as the editor's choice, being granted free access to all users and selected to stamp the journal's cover page.

The first operator yielded high accuracy performing noise injection to DM images, as seen in [30]. However, applications such as tomosynthesis and computed tomography (CT) operate at lower photon fluence ranges, and thus some of the assumptions required by the first operator are not fulfilled. A preliminary study was conducted to explore the direct application of the method presented in [30] to DBT images. The results are organized in [31], which was published by the *Lecture Notes in Computer Science*, by Springer, and presented at the *International Workshop in Digital Mammography*. The paper was selected among the 5 best student papers in the conference and was awarded the National Institutes of Health and National Cancer Institute student fellowship. Although the results were promising, the operator yielded higher errors compared to [30].

Next, the operator was optimized to perform accurate noise injection in low photon fluence applications. The optimization was achieved by modifying the coefficients of the VST to minimize the errors in the variance and expectation of the simulated distribution. This new operator was demonstrated and validated using hypothetical signals and fluorescence images. The formalization and validation are organized in [29], which was published by the *IEEE Signal Processing Letters* journal. This journal has high reputation and visibility in the signal processing field (Impact Factor: 2.528), and is classified as A1 by the CAPES Qualis rank.

Even with high performance at low photon fluence, two other aspects needed to be considered in our noise injection operator before the application to DBT images: the electronic noise and the pixel crosstalk. The electronic noise is caused by the random fluctuations in the electronics of the system and can be described by a signal-independent Gaussian distribution. The pixel crosstalk is caused by physical aspects of the system, such as electron drift, and it causes the noise to be frequency-dependent (non-white). Thus, the pure white Poisson model is no longer adequate for this application, and

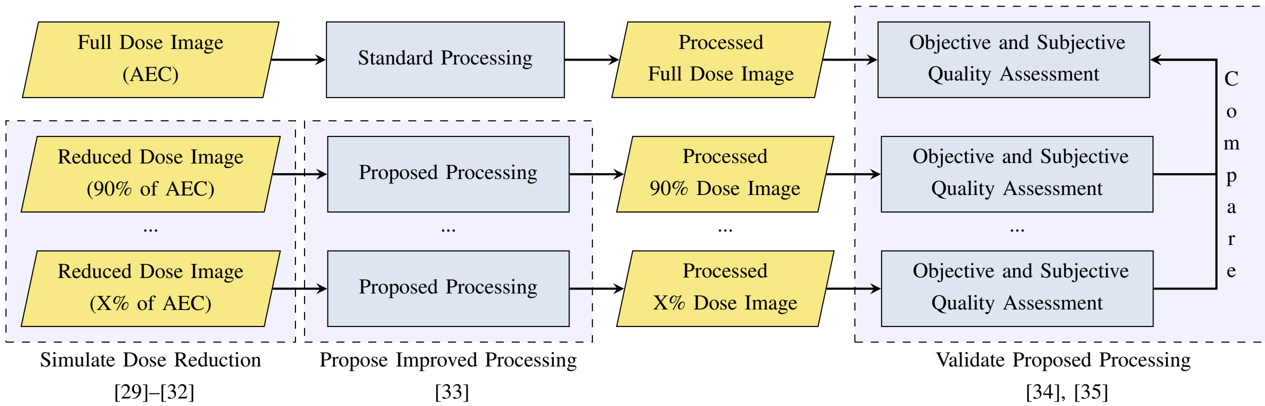

Fig. 1. Flowchart of the study performed in the thesis, with references to the corresponding publications. AEC stands for 'Automatic Exposure Control'.

a Poisson-Gaussian model must be adopted.

The new operator was inspired by the Generalized Anscombe Transformation (GAT), which is a VST for Poisson-Gaussian variables. The injection was performed in the variance-stabilized range, similarly to the previous operators. Furthermore, an additional step was performed to create noise correlation, which simulates the pixel crosstalk.

In our previous publications, the evaluation of the simulation method was performed using anthropomorphic phantoms, which mimics the anatomical and physical aspects of the human breast. The use of phantoms allowed the estimation of a ground-truth image, and thus objective metrics of similarity were used to compare statistics of the simulated and real images. Once more the physical phantoms were used for the validation of the third operator. However, in addition to objective measurements, a human observer experiment was conducted. In this experiment, medical physicists evaluated a set of phantom images to assess the similarity of the noise strength in real and simulated images. The subjective evaluation using human observers is closer to the real clinical task in image interpretation, and therefore is an important aspect to be investigated.

The formalization and validation of the third operator are presented in [32]. The work was published by *IEEE Transactions in Medical Imaging*. This journal is relevant to the medical imaging and signal processing fields (Impact Factor: 3.94), and is classified as A1 in the CAPES Qualis rank.

After developing and validating the operators used to simulate dose reduction DBT images, the second part of the thesis focused in the clinical application of the method. The goal is to investigate the feasibility of restoring DBT images, acquired at lower radiation levels, to achieve a similar SNR regime as full-dose acquisitions.

First, a denoising pipeline was proposed. A Poisson-Gaussian model was adopted, and particularities such as spatially varying quantum gain, pixel offset and electronic noise were considered. Furthermore, an appropriate VST allowed the use of "off-the-shelf" state-of-the-art denoising techniques developed for Gaussian variables. The pipeline was formalized and validated using DM and DBT phantom images. The results are organized in [33]. The work was submitted and presented at the *2017 SPIE Medical Imaging Conference*, and was awarded second place on the best student paper in Physics.

To achieve the SNR of full-dose acquisitions, DBT projections acquired at low-dose were denoised and a weighted-average was used to inject the denoised signal into the noisy signal. This process avoids the excessive signal smoothing found in denoised images. The final evaluation was divided into two components: the objective validation was performed using quality metrics and presented in [34]. The work was published by the Measurement Science and Techlonogy journal, in a special issue on Advanced x-ray Tomography. This journal has relevant visibility in the international community (Impact Factor: 1.68) and is classified as A2 in the CAPES Qualis rank. The second portion, detailed in [35], contains a 2-AFC human observer experiment used to compare the noise and blur levels from restored low-dose and full-dose acquisitions. The work was submitted and presented at the *2018 SPIE Medical Imaging Conference*.

III. Conclusions

In the Ph.D. thesis, we presented and validated an image restoration framework capable of recovering DBT images acquired at low radiation doses, to achieve the SNR regime of full-dose acquisitions.

The objective and subjective evaluation of the image restoration framework indicate that 30% to 50% of dose reudction could be achieved, with no relevant changes in image quality, when the proposed restoration framework was applied.

Awards, Publications and Distinctions

Other scientific awards, publications and distinctions are related to this Ph.D.:

- **Book Chapter:** Azzari, L.; Borges, L.R.; Foi, A. Modeling and Estimation of Signal-Dependent and Correlated Noise. In: *Denoising of Photographic Images and Video*, Springer International Publishing, In Print. Available at: https://www.springer.com/gp/book/9783319960289

- **Journal:** Borges, L.R.; Barufaldi, B.; Caron, R.F.; Bakic, P.; Maidment, A.D.A.; Vieira, M.A.C. Noise Models in Virtual Clinical Trials of Digital Breast Tomosynthesis. *Submitted to Medical Image Analysis*.
- **Journal:** Bria, A.; Marrocco, C.; Borges, L.R.; Molinara, M.; Marchesi, A.; Mordang, J-J; Karssemeijer, N.; Tortorella, F. Improving the Automated Detection of Calcifications using Adaptive Variance Stabilization. *IEEE Transactions on Medical Imaging*, In Print. Available at: https://doi.org/10.1109/TMI.2018.2814058
- **Proceedings:** Brito, F. A.; Borges, L.R.; Guerrero, I.; Bakic, P.R.; Maidment, A.D.A.; Vieira, M.A.C. Application of neural networks to model the signal-dependent noise of a digital breast tomosynthesis unit. In: *Proceedings of the SPIE Medical Imaging 2018: Physics of Medical Imaging*, Houston, 2018.
- **Proceedings:** Borges, L.R.; Bakic, P.R.; Maidment, A.D.A.; Vieira M.A.C. Metal Artifact Reduction using a patch-based reconstruction for digital breast tomosynthesis. In: *Proceedings of the SPIE Medical Imaging 2017: Physics of Medical Imaging*, Orlando, 2017.
- **Proceedings:** Oliveira, H.C.R.; Moraes, D.R.; Reche, G.A.; Borges, L.R.; Catini, J.H.; Barros, N.; Melo, C.F.E.; Gonzaga, A.; Vieira M.A.C. A New Texture Descriptor Based on Local Micro-Patter for Detection of Architectural Distortion in Mammographic Images. In: *Proceedings of the SPIE Medical Imaging 2017: Physics of Medical Imaging*, Orlando, 2017.
- **Proceedings:** Barufaldi, B.; Borges, L.R.; Bakic, P.R.; Vieira, M.A.C.; Schiabel, H.; Maidment, A.D.A. Assessment of automatic exposure control performance in digital mammography using a no-reference anisotropic quality index. In: *Proceedings of the SPIE Medical Imaging 2017: Physics of Medical Imaging*, Orlando, 2017.
- **Proceedings:** Barufaldi, B.; Borges, L.R.; Bakic, P.R.; Vieira, M.A.C.; Schiabel, H.; Maidment, A.D.A. Assessment of automatic exposure control performance in digital mammography using a no-reference anisotropic quality index. In: *Proceedings of the SPIE Medical Imaging 2017: Physics of Medical Imaging*, Orlando, 2017.
- **Proceedings:** Guerrero, I.; Borges, L.R.; Vieira, M.A.C. Correção do Espectro de Potência do Ruído na Simulação de Redução da Dose de Radiação em Imagens de Tomossíntese Digital Mamária. *Proceedings of the Congresso Brasileiro de Física Médica*, Ribeirão Preto, 2017.
- **Proceedings:** Borges, L.R.; Guerrero, I.; Bakic, P.R.; Maidment, A.D.A.; Vieira, M.A.C. Gaussian-Poisson noise estimation from individual mammography images. In: *Proceedings of the Workshop de Visão Computacional*, Campo Grande, 2016.
- **Proceedings:** Nunes, P.F.; Bindilatti, A.A.; Oliveira, H.C.R.; Borges, L.R.; Bakic, P.R.; Maidment, A.D.A.; Mascarenhas, N.D.A.; Vieira, M.A.C. Nova proposta do algoritmo de médias não-locais para filtragem de ruído quântico na mamografia digital. In: *Proceedings of the Congresso Brasileiro de Engenharia Biomédica*, Foz do Iguaçú, 2016.
- **Proceedings:** Barufaldi, B.; Borges, L.R.; Vieira, M.A.C.; Gabarda, S.; Maidment, A.D.A.; Bakic, P.R.; Pokrajac, D.D.; Schiabel, H. The Effect of Breast Composition on a No-reference Anisotropic Quality Index for Digital Mammography. In: Anders Tingberg; Kristina Lang; Pontus Timberg. *Breast Imaging*. 1ed.: Springer, v. 9699, p. 226-233, 2016.
- **Proceedings:** Oliveira, H.C.R.; Barufaldi, B.; Borges, L.R.; Gabarda, S.; Bakic, P.R.; Maidment, A.D.A.; Schiabel, H.; Vieira, M.A.C. The Effect of Breast Density on a No-reference Anisotropic Quality Index for Digital Mammography. In: *Proceedings of the SPIE Medical Imaging 2016: Image Perception*, San Diego, 2016.
- **Proceedings:** Borges, L.R.; Vieira, M.A.C.; Foi, A. Unbiased Noise Injection in Variance-Stabilized Range. In: *Proceedings of the SIAM Conference on Imaging Science*, Albuquerque, 2016.
- **Proceedings:** Borges, L.R.; Vieira, M.A.C.; Foi, A. Unbiased Injection of Signal-Dependent Noise in Variance-Stabilized Range. In: *Proceedings of the IEEE Workshop on Statistical Signal Processing*, Palma de Mallorca, 2016.
- **Proceedings:** Borges, L.R.; Hwuang, E.; Acciavatti, R. J.; Vieira, M. A. C.; Maidment, A. D. A. Tomosynthesis Reconstruction Based on Principal Component Analysis (PCA). In: *Radiological Society of North America*, 2016, Chicago, 2016.
- **Distinction:** Invited Conference Chair, Gordon Research Seminars on Image Science, Boston, USA, 2018.
- **Distinction:** Invited Speaker, Food and Drugs Administration, Washington, USA, 2017.
- **Award:** Second Best Student Physics Paper, SPIE Medical Imaging, Orlando, EUA, 2017.
- **Award:** Santander Universities Award, Guildford, United Kingdom, 2017.
- **Award:** Student Grant Award, Radiological Society of North America, Chicago, USA, 2017.
- **Award:** One year as a visiting Ph.D. student at the University of Pennsylvania, Philadelphia, USA. Science without Borders, CAPES, 2016.
- **Award:** Honorable Mention, American Association of Physics in Medicine, Philadelphia, USA, 2016.
- **Award:** Student Travel Grant, Gordon Research Conference on Image Science, Boston, USA, 2016.
- **Award:** Student Fellowship, International Workshop on Breast Imaging, Mälmo, Sweden, 2016.
- **Award:** Student Travel Grant, SPIE Medical Imaging, San Diego, USA, 2016.
- **Distinction:** Featured Paper, Medical Physics, 2016.
- **Distinction:** Visiting researcher at Tampere University of Technology, Tampere, Finland. Funded by the Academy of Finland, 2015.

ACKNOWLEDGMENTS

This work was supported by the São Paulo Research Foundation (FAPESP grants no. 2013/18915-5 and 2016/25750-0), and by the Brazilian Foundation for the Coordination of Improvement of Higher Education Personnel (CAPES grant no. 88881.030443/2013-01). The authors would like to thank Dr. Predrag Bakic and Dr. Andrew Maidment, from the University of Pennsylvania, and Dr. Alessandro Foi, from Tampere University of Technology, for their support in this project.

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