



# Intercomparison of quality control software responses in measuring the modulation transfer function in mammography

Almeida <sup>a\*</sup>, L. F. M.; Squair <sup>a</sup>, P. L.; Nogueira <sup>a</sup>, M. S.

<sup>a</sup> Centro de Desenvolvimento da Tecnologia Nuclear, 31270-901, Belo Horizonte-MG, Brazil.

\*Correspondence: lailafernanda8852@gmail.com

**Abstract:** The National Cancer Institute (INCA) estimated approximately 74,000 new cases of breast cancer in Brazil in 2023, making it the second most common cancer among women. Mammography is the most effective method for early diagnosis, capable of detecting lesions as small as 2 mm before symptoms or dissemination. To ensure its effectiveness, mammography systems must comply with Brazilian standards, such as RDC n° 611 and IN n° 92 from Anvisa, through quality control testing. One of the primary quality tests is the Modulation Transfer Function (MTF) analysis, which evaluates system performance in the spatial frequency domain to ensure diagnostic accuracy. This study assessed the performance of three software tools — ATIA, COQ, and MAMMOQC — in analyzing the MTF of digital mammography systems, focusing on Retrofit DR and CR technologies. Images were acquired using a Siemens Mammomat 3000 NOVA analog mammograph equipped with a Retrofit DR detector and a CR plate. Digital images were analyzed using ATIA, which automatically positions Regions of Interest (ROIs), and the COQ and MAMMOQC plugins in ImageJ, where ROIs were manually selected. MTF values at 10%, 20%, and 50% were compared between the software using paired t-tests with a 5% significance level. Results showed that ATIA and MAMMOQC exhibited higher agreement for 50% MTF, while COQ often produced higher resolution values, particularly at 10% and 20% MTF, highlighting methodological differences among the tools. Statistical analysis revealed significant discrepancies between software results, particularly for the CR system. For the Retrofit DR system, significant variability was observed in comparisons between COQ and MAMMOQC ( $p = 0.030$ ). For the CR system, all software comparisons showed significant differences, suggesting greater sensitivity to noise and methodological variations at lower MTF percentages. These findings underscore the importance of understanding the strengths and limitations of each software for mammography quality control and emphasize the need for further validation of ATIA as a reliable tool in this field.

**Keywords:** Modulation Transfer Function, Mammography, Quality Control, ATIA.



# Intercomparação da resposta de softwares de controle de qualidade na medição da função de transferência de modulação em mamografia

**Resumo:** O Instituto Nacional de Câncer (INCA) previu cerca de 74.000 novos casos de câncer de mama no Brasil em 2023, tornando-o o segundo mais comum entre mulheres. Diante disso, a mamografia é o método mais eficaz para diagnóstico precoce, detectando lesões de até 2 mm antes de sintomas ou disseminação. Dessa forma, para garantir sua eficiência, os mamógrafos devem atender às normas brasileiras, como a RDC nº 611 e a IN nº 92 da Anvisa, por meio de testes de controle de qualidade. Um dos principais testes de qualidade é a análise da Função de Transferência de Modulação (MTF), que avalia o desempenho do sistema no domínio da frequência espacial, assegurando diagnósticos precisos. Dessa forma, este estudo avaliou o desempenho de três ferramentas de software — ATIA, COQ e MAMMOQC — na análise da MTF em sistemas de mamografia digital, especificamente nas tecnologias Retrofit DR e CR. A aquisição das imagens foi realizada utilizando um mamógrafo analógico Siemens Mammomat 3000 NOVA com detector Retrofit DR e uma placa CR. As imagens digitais foram analisadas com o ATIA, que posiciona automaticamente as regiões de interesse (ROIs), e com os plugins COQ e MAMMOQC no ImageJ, onde as ROIs foram selecionadas manualmente. Os valores de MTF em 10%, 20% e 50% foram comparados entre os softwares por meio de testes t pareados com nível de significância de 5%. Os resultados mostraram que ATIA e MAMMOQC apresentaram maior concordância para a MTF de 50%, enquanto o COQ frequentemente apresentou valores de resolução mais elevados, especialmente em 10% e 20% de MTF, destacando diferenças metodológicas entre as ferramentas. A análise estatística revelou discrepâncias significativas entre os resultados dos softwares, particularmente no sistema CR. Para o sistema Retrofit DR, foi observada variabilidade significativa na comparação entre COQ e MAMMOQC ( $p = 0,030$ ). Para o sistema CR, todas as comparações entre os softwares mostraram diferenças significativas, sugerindo maior sensibilidade ao ruído e variações metodológicas em porcentagens menores de MTF. Esses achados ressaltam a importância de compreender os pontos fortes e as limitações de cada software para o controle de qualidade em mamografia, além de destacar a necessidade de validação adicional do ATIA como ferramenta confiável nesse campo.

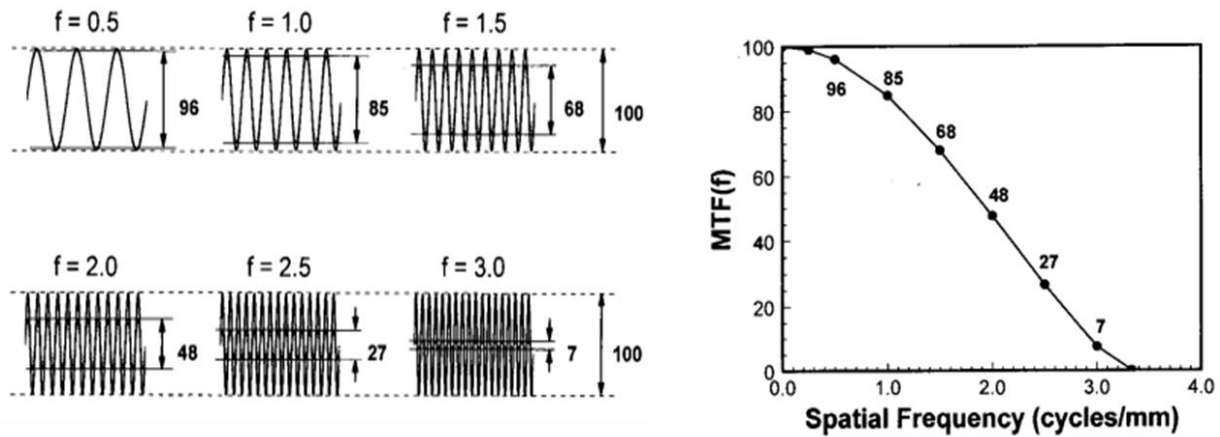
**Palavras-chave:** Função de Transferência de Modulação, Mammography, Quality Control, ATIA.

## 1. INTRODUCTION

The National Cancer Institute (INCA) predicts that, between 2023 and 2025, breast cancer will be the second most common type among women in Brazil, with an estimated 74,000 new cases in 2023 alone [1]. In this context, mammography is considered the most effective method for early disease diagnosis, as it can detect lesions as small as 2 mm before symptoms appear or the disease spreads [2]. To ensure the efficiency of this exam, it is essential that mammographs and their components comply with current standards, regulatory agency guidelines, and applicable resolutions. In Brazil, these include the Collegiate Board Resolution n° 611 and Normative Instruction n° 92, both from the National Health Surveillance Agency (Anvisa) [3,4]. Among the tests that evaluate equipment quality, the analysis of the Modulation Transfer Function (MTF) stands out, measuring system performance in the spatial frequency domain [5].

MTF quantitatively assesses the ability of an optical or imaging system to preserve contrast in details as it transfers information from a scene to the formed image. This function graphically represents the relationship between the spatial frequency of the observed object and the contrast in the final image, as shown in Figure 1. The image includes six sinusoidal waves with spatial frequencies ranging from 0.5 to 3.0 line pairs per millimeter (lp/mm). Initially, the amplitude (or contrast) is 100%, but as spatial frequency increases (details become smaller), the amplitude decreases, showing how contrast is lost. In the graph on the right, this is represented by the curve dropping as frequency increases, indicating a loss of quality at higher frequencies due to "blurring" [6].

**Figure 1:** Representation of spatial frequencies in relation to the MTF of a system.



Source: Bushberg *et al.*, 2001.

Simplified, MTF analyzes how the system maintains or reduces contrast across different spatial frequencies. Additionally, it provides insight into the system's response to specific frequencies, making it useful for determining spatial resolution. Systems with higher MTF values exhibit less blur and greater ability to identify fine details, such as microcalcifications in breast tissue. MTF is generally calculated using the edge method, where software analyzes the equipment's response to a sharp edge pattern, determining the quality of the generated image [6,5]. Equation 1 is used for MTF calculation [6,7].

$$MTF(f) = \left| \int_{\chi=-\infty}^{\infty} LSF(\chi) e^{-2\pi i f \chi} d\chi \right| \quad (1)$$

Where,  $MTF(f)$  represents the Modulation Transfer Function as a function of spatial frequency,  $\int_{\chi=-\infty}^{\infty} LSF(\chi)$  it indicates that the integration is performed over the entire extent of space in the integration variable ( $\chi$ ),  $LSF(\chi)$  is the Line Spread Function and measures the dispersion of light intensity around this line due to aberrations and diffraction, and  $e^{-2\pi i f \chi}$  represents the basis of the Fourier Transform, used to convert the spatial function  $LSF(\chi)$  into the frequency domain, while  $d\chi$  indicates the integration along the entire spatial coordinate  $\chi$ .

ImageJ, using the COQ and MAMMOQC plugins, is a commonly used software for this analysis, allowing manual insertion of regions of interest and obtaining MTF and resolution values. To automate this task and provide more precise results, the International Atomic Energy Agency (IAEA) developed the Automated Tool for Image Analysis (ATIA) in 2021, as described in Human Health Series No. 39. This open-source and free software is designed for quality control in mammography and radiography and is available on the IAEA Human Health Campus website [7]. However, as this methodology is relatively recent, there are still few studies focused on mammography that compare the IAEA software's response with other established tools for analyzing diagnostic imaging equipment.

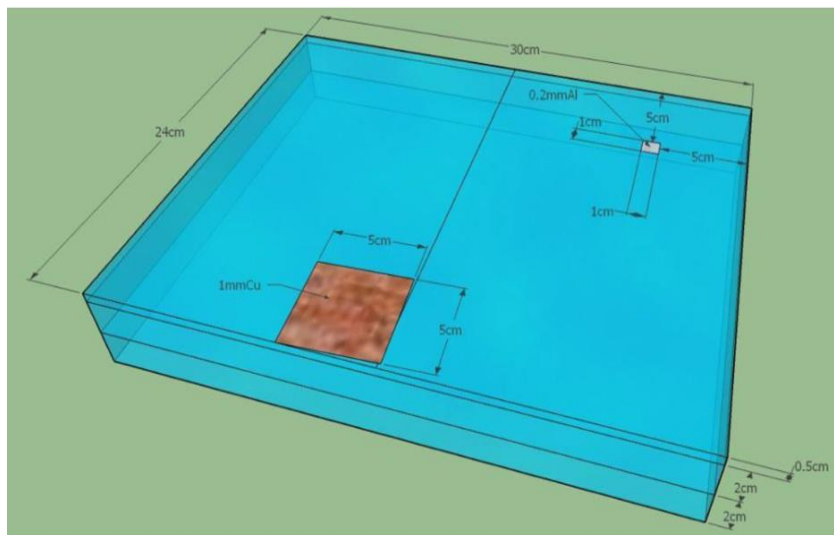
So far, there is only one study, by Fogagnoli *et al.* (2022) [8], that compares the responses obtained for various metrics in mammography, including MTF, between the ImageJ software with the COQ Plugin and ATIA. In addition to this, there are two other studies related to the use of ATIA in mammography equipment. The study by Mora *et al.* (2021) [9] proposed and validated the methodology described by the IAEA, conducting a pilot project for its implementation, although it does not compare the responses with other quality control software. The study by Fitton *et al.* (2024) [10] investigated the impact of two-dimensional (2D) mammographic acquisition techniques on image quality and radiation dose in the presence of silicone breast implants, using the IAEA standard simulator and ATIA software, but, like the study by Mora *et al.* (2021), it did not compare the results with other quality control software.

Therefore, this study aims to analyze the accuracy of the ATIA software in evaluating the Modulation Transfer Function (MTF) in horizontal and vertical orientations in mammography. For this purpose, a comparison will be conducted between ATIA and the COQ and MAMMOQC plugins from ImageJ, based on MTF values at 10%, 20%, and 50%, providing a detailed assessment of each software's performance.

## 2. MATERIALS AND METHODS

Firstly, to use the ATIA software, a mammography phantom was fabricated according to the IAEA's methodological requirements. It consisted of two parts, as shown in Figures 2 and 3. The first part includes four uniformly attenuating polymethylmethacrylate (PMMA) plates, each measuring 24 x 30 x 1 cm. The second part comprises a PMMA target plate with dimensions of 24 x 30 x 0.5 cm, containing a square copper (Cu) piece measuring 5 x 5 cm and 1 mm thick, along with an aluminum (Al) piece measuring 1 x 1 cm and 0.2 mm thick [7].

**Figure 2:** Dimensions of the standard mammography simulator/phantom developed by the IAEA.



Source: IAEA, 2021.

**Figure 3:** Standard phantom/simulator manufactured according to the IAEA methodology.



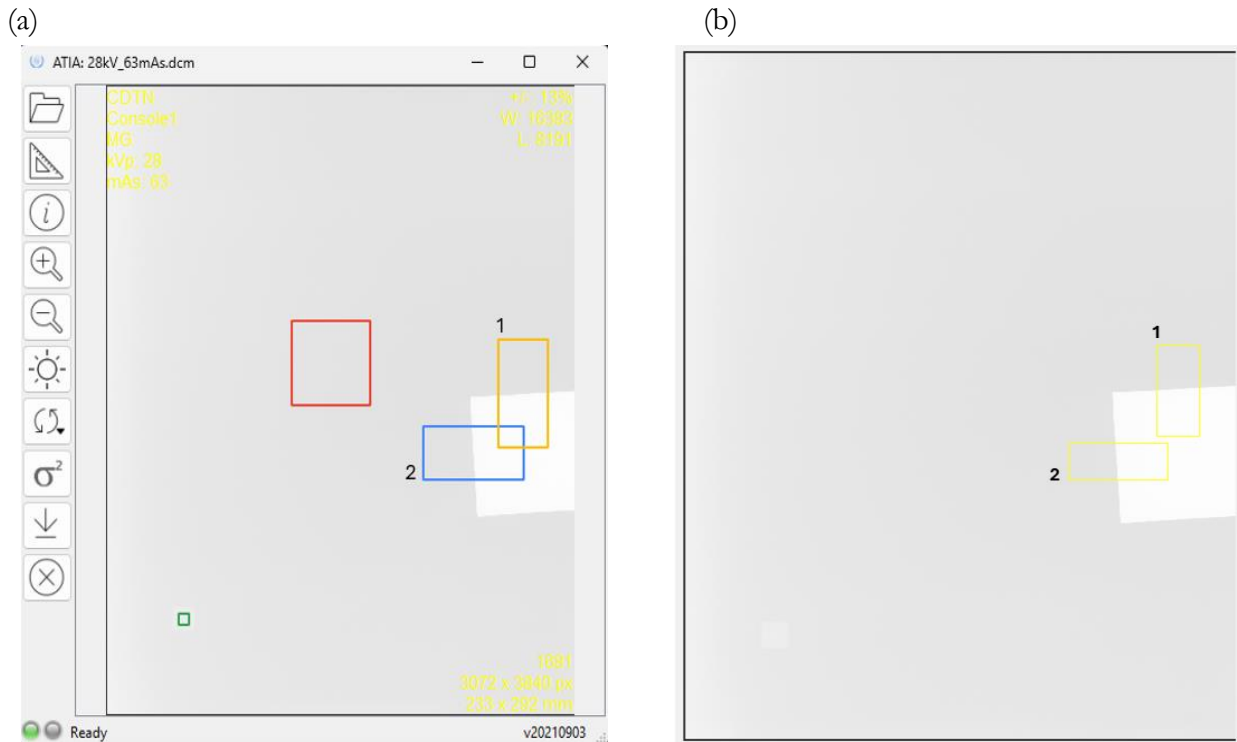
Source: Author's archives.

The images were acquired using a digital detector and a computed radiography (CR) imaging plate. A Shimadzu Retrofit DR digital detector, model RoseM (RSM 2430C), designed for digital X-ray imaging in mammography and compatible with general-purpose analog systems, was employed [11]. The CR system used was the Kodak Direct View [12]. Both detectors were attached to a Siemens analog mammography system, model Mammomat 3000 NOVA [13]. The images were acquired using a molybdenum-molybdenum (MoMo) target-filter combination, with a voltage (kVp) of 28 and a constant load of 63 mAs on both systems [12,14,15].

Subsequently, the digital images (in DICOM and Raw Data formats) were input into the ATIA software, which automatically positioned the Regions of Interest (ROIs) and performed automated measurements. The images were then processed using the COQ and MAMMOQC plugins in the IMAGEJ software, where the same ROIs used in ATIA were manually positioned in both vertical and horizontal orientations, with dimensions of 50 x 25 mm for COQ and 40 x 40 mm for MAMMOQC. All MTF percentages present in the image were obtained. For cases where the values of interest at 10%, 20%, and 50% were not found, interpolation was performed to determine the most precise value [7,9].

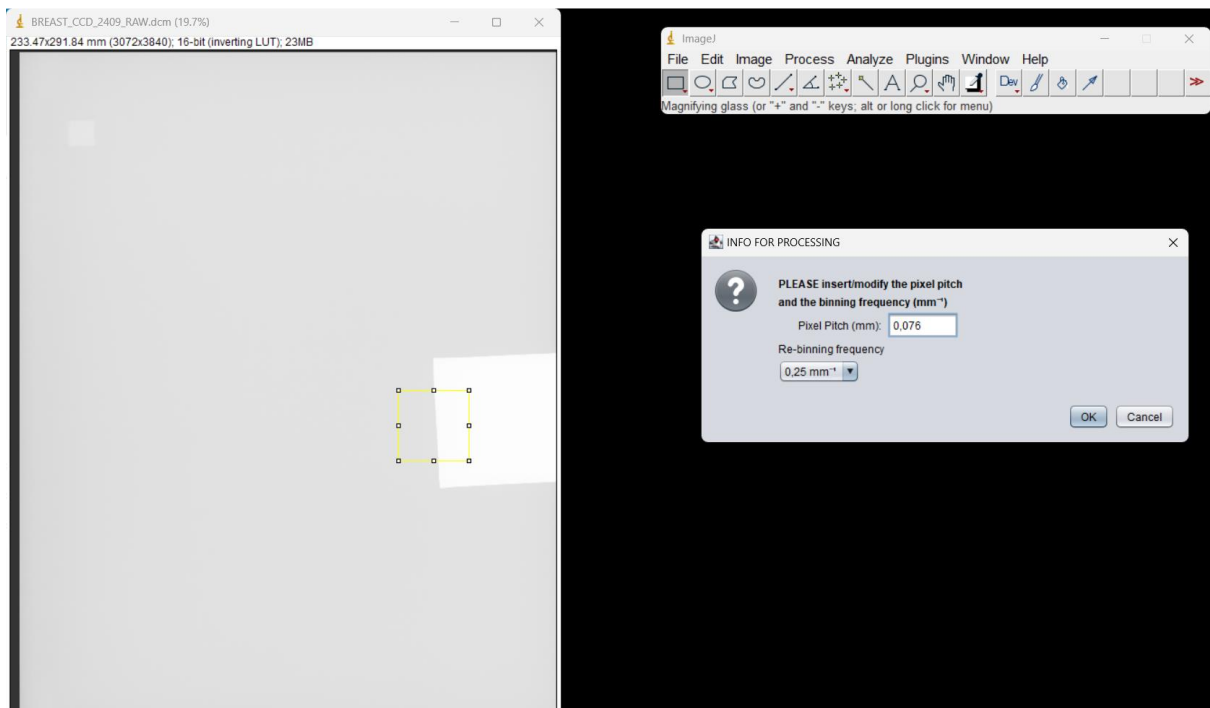
Figure 4 (a) shows the image input into ATIA, with ROIs 1 and 2 corresponding to MTFs for vertical and horizontal edges, using Fourier transform on sharp-edged images, and 4 (b) displays the image input into the COQ plugin of ImageJ with manually positioned ROIs. Figure 5 shows the image input into the MAMMOQC plugin of ImageJ with the ROI on the edge of interest [14, 16].

**Figure 4:** Raw Data image input into ATIA (a) with automatically positioned ROIs and Raw Data image input into the COQ plugin of ImageJ with manually positioned ROIs.



Source: Almeida *et al.*, 2024<sup>b</sup>.

**Figure 5:** Raw Data image input into the MAMMOQC plugin of ImageJ with manually positioned ROI.



Source: Author's archives.



For data comparison, Minitab version 18 statistical software was used to perform paired T-tests with a 5% significance level. The null hypothesis stated that there was no significant difference between population means, while the alternative hypothesis suggested insufficient evidence to conclude that the mean difference between paired observations was statistically significant. Additionally, the means and standard deviations of the differences between the software were analyzed [17].

### 3. RESULTS AND DISCUSSIONS

The following MTF values were obtained for the Retrofit DR and CR systems (Tables 1 and 2). Based on these data, the necessary statistics were constructed.

**Table 1:** MTF values obtained for the Retrofit DR system across different quality control software.

MTF (%)	Resolution (mm <sup>-1</sup> )		
	ATIA	COQ	MAMMOQC
50% Horizontal	2.08	2.19	1.78
20% Horizontal	4.21	4.76	4.00
10% Horizontal	5.61	4.97	2.39
50% Vertical	2.06	2.12	1.73
20% Vertical	3.11	4.12	3.25
10% Vertical	5.52	5.47	4.50

**Table 2:** MTF values obtained for the CR system across different quality control software.

MTF (%)	Resolution (mm <sup>-1</sup> )		
	ATIA	COQ	MAMMOQC
50% Horizontal	1.18	1.90	0.90
20% Horizontal	2.91	3.89	2.00
10% Horizontal	3.99	4.99	2.59
50% Vertical	1.00	1.83	0.85
20% Vertical	2.90	3.69	1.75
10% Vertical	3.95	4.59	2.54

The presented data show that the Retrofit DR system exhibits higher MTF values compared to CR across all directions and spatial frequencies, highlighting its greater ability to capture fine details. The lower resolution of the CR system can be explained by several technical factors. This system uses photostimulable phosphor plates to store the image, which is later read by a laser beam. This process causes light dispersion, reducing image sharpness. Additionally, CR detectors are larger and less efficient in directly converting radiation into a digital signal, whereas DR employs smaller and more precise sensors. Another limitation of CR is the need for multiple stages to convert light information into a digital signal, which can increase noise and reduce the final image quality [5,6].

The superiority of DR is particularly evident at higher spatial frequencies, where contrast and definition are essential for detecting small structures such as microcalcifications in mammography. This more efficient performance makes Retrofit DR a better choice for high-precision examinations, while CR, due to optical losses and limitations in the image capture and conversion process, has lower resolution and a reduced ability to highlight fine details [5,6].

### 3.1. Graphical Analysis

Figure 6 (a) presents a scatter plot of the MTF results for the Retrofit DR plate image. It can be observed that the three software analyzed exhibited a response variability of less than 0.5 in spatial resolution for 50% MTF (in both horizontal and vertical directions). However, at lower percentages, the results showed greater variation between them, with differences of up to 2.5.

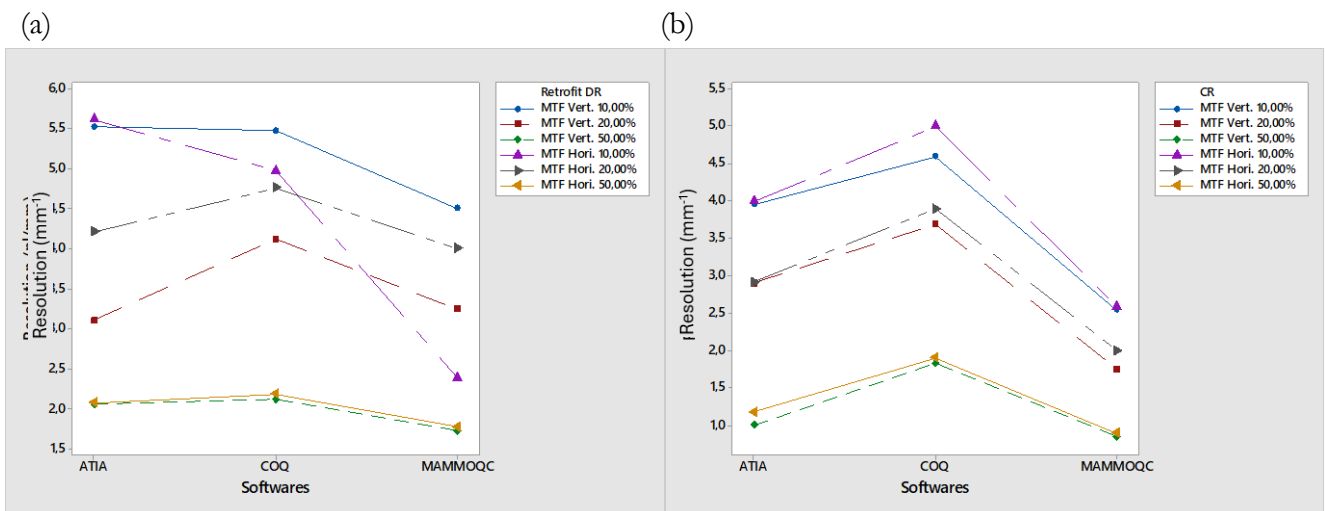
For the 20% MTF (horizontal and vertical), the values obtained by the ATIA and MAMMOQC software were similar, while COQ showed higher resolution values, diverging from the others. For the 10% MTF (horizontal and vertical), the differences between the software were even more significant, except for the vertical MTF, where ATIA and COQ showed almost identical responses.

These data indicate differences in precision and agreement between the software, depending on the modulation level analyzed. Moreover, the higher variation observed at the 10% MTF can be explained by the concepts of Bushberg *et al.* (2011), as this metric indicates the minimum resolution limit that a system can generate, making it more susceptible to image noise [6].

Figure 6 (b) presents a scatter plot of the MTF results for the CR plate image, demonstrating variability differences between the analyzed software. For 50% MTF (horizontal and vertical), the results of the ATIA and MAMMOQC software showed relatively good agreement, with little variation in spatial resolution values, while COQ exhibited relatively higher values.

However, at lower modulation percentages, such as 20% MTF (horizontal and vertical), greater dispersion was observed among the results, with COQ showing the highest resolution values, while MAMMOQC displayed the lowest. At 10% MTF (horizontal and vertical), the differences between the software became even more evident, with COQ again standing out with the highest resolution values, while ATIA and MAMMOQC showed lower and more divergent values.

**Figure 6:** Scatter plot of MTF, horizontal and vertical, for a Retrofit DR plate (a) and for a CR system (b).



Source: Author's archives.

These results, for both systems, align with the findings of Fogagnoli *et al.* (2023), where the calculated MTFs differed from the values provided by ATIA, especially for higher spatial frequencies [8]. It is important to note that the same edge method was used in all the software; however, these differences can be attributed to the data processing method. In the ImageJ software, it is necessary to input the detector's linearized response function (especially if it is a system with a logarithmic response, such as the CR system) for the MTF to be correctly calculated. On the other hand, the ATIA software performs the calculations automatically without data linearization. This directly implies a change in the results.

### 3.2. Analysis of Paired Difference Estimates and p-Values

The analysis of Paired Difference Estimates provides the mean differences between measurements from the three software and the standard deviation, allowing for understanding the direction and magnitude of the differences. The "p" values indicate the probability that the observed differences are due to chance. Thus, "p" values below 0.05 are considered statistically significant, rejecting the null hypothesis. This means that the difference between the population means is not equal to the hypothesized difference, indicating significant response differences among the software. Table 3 presents the analysis of paired differences and "p" values among the three software tools.

**Table 3:** Analysis of Paired Differences and p-Values among the software.

Softwares \ Technology	Retrofit DR		CR	
	Mean ± Standard Deviation	p-value	Mean ± Standard Deviation	p-value
ATIA-COQ	-0.175 ± 0.561	0.479	-0.828 ± 0.141	0.000
ATIA-MAMMOQC	0.822 ± 1.232	0.163	0.822 ± 0.551	0.011
COQ-MAMMOQC	0.997 ± 0.811	0.030	1.710 ± 0.587	0.001

The table analysis allows us to conclude that the highest standard deviation values were observed in comparisons between ATIA-MAMMOQC (Retrofit DR) and COQ-MAMMOQC (CR), with values of 1.232 and 0.587, respectively. On the other hand, the

lowest variability was recorded in comparisons between ATIA-COQ for both technologies, being 0.561 for the Retrofit DR and 0.141 for the CR.

Regarding p-values, the results indicate that, for the Retrofit DR system, a statistically significant difference was found in the comparison between COQ-MAMMOQC ( $p = 0.030$ ). For the CR system, all comparisons showed statistically significant differences in responses, highlighting relevant discrepancies among the analyzed methods.

## 4. CONCLUSIONS

Based on the results found, it can be inferred that, in the evaluation of the metric, the Retrofit DR system presents a higher MTF compared to CR, capturing finer details, especially at higher spatial frequencies, which are essential for detecting microcalcifications. The lower resolution of CR is due to light dispersion in the phosphor plates and the indirect signal conversion process, while DR uses more precise sensors, making it more effective for high-precision examinations.

The graphical analysis showed variations between the software analyzed for both systems, especially at higher spatial frequencies. For 50% MTF, there was good agreement between ATIA and MAMMOQC, while COQ frequently showed higher resolution values. However, for 20% and 10% MTF, the divergence between the software increased, with COQ demonstrating higher resolution. These discrepancies align with the findings of Fogagnoli *et al.* (2023) and can be attributed to differences in data processing methods. While ImageJ requires the insertion of the detector's linearized response function, ATIA, being designed for full automation, does not request this function, directly impacting the results and potentially providing erroneous values in quality control practice, as it does not take into account the detector's response type for final analysis.

The analysis of Paired Differences revealed significant variations between the software, especially for the CR system, where all comparisons showed "p" values below 0.05, indicating statistically significant differences in responses. For Retrofit DR, the greatest discrepancy was observed between COQ and MAMMOQC ( $p = 0.030$ ). The largest standard deviations occurred in the ATIA-MAMMOQC (Retrofit DR) and COQ-MAMMOQC (CR) comparisons, while the lowest variability was recorded between ATIA-COQ for both systems. Therefore, due to the observed discrepancies, further studies are necessary to evaluate the accuracy of the ATIA software under different parameters.

## ACKNOWLEDGMENT

This work was supported by the following organizations: the Brazilian National Council for Scientific and Technological Development (CNPq - Master's Scholarship), the Brazilian Institute of Science and Technology in Nuclear Instrumentation and Applications to Industry and Health (INCT/INAIS - Project 406303/2022-3 and CNPq Process 308368/2022-3 – Productivity Fellowship), the Minas Gerais State Research Support Foundation (FAPEMIG), and the Nuclear Technology Development Center (CDTN).

## CONFLICT OF INTEREST

The authors of this article declare that there are no conflicts of interest, financial or otherwise, that could have influenced the results or conclusions presented. All data and analyses were conducted objectively, aiming to contribute to the advancement of scientific knowledge in the relevant field.

## REFERENCES

- [1] INCA, Instituto Nacional de Câncer José Alencar Gomes da Silva. Estimativa 2023: incidência de câncer no Brasil. **Ministério da Saúde**. Rio de Janeiro, p. 162, 2022.
- [2] BIASOLI JR, A. Técnicas radiográficas: princípios físicos, anatomia básica, posicionamento, radiologia digital, tomografia computadorizada. **Rubio**, Rio de Janeiro, 2. Ed, 2016.
- [3] BRAZIL. Ministério da Saúde. Diretoria Colegiada da Agência Nacional de Vigilância Sanitária. Instrução Normativa IN Nº 92, de 27 de maio de 2021. Brasília, DF: **Diário Oficial da União**, 2021.
- [4] BRAZIL. Ministério da Saúde. Diretoria Colegiada da Agência Nacional de Vigilância Sanitária. RDC Nº 611, de 9 de março de 2022. Brasília, DF: **Diário Oficial da União**, 2022.
- [5] SEFM-SEPR-SERAM, Protocolo Español de Control de Calidad en Radiodiagnóstico. **Editora Senda S.A.**, 2011.
- [6] BUSHBERG, J.T. *et al.* The essential physics of medical imaging. **Lippincott Williams & Wilkins**, Philadelphia, 2 ed., 2001.
- [7] IAEA - International Atomic Energy Agency. Implementation of a Remote and Automated Quality Control Programme for Radiography and Mammography Equipment. Vienna: Human Health Series nº39. Disponível em: <https://www.iaea.org/publications/13539/implementation-of-a-remote-and-automated-quality-control-programme-for-radiography-and-mammography-equipment>. Acesso em: 30 dez. 2024.
- [8] FOGAGNOLI, M. P. *et al.* Implementação de um Programa de Controle de Qualidade Remoto para Avaliação de Imagens em Radiografia Convencional e Mamografia. **Revista Brasileira de Física Médica**, São Paulo, v. 16, p. 696-696, 2022.
- [9] MORA, P. *et al.* The IAEA remote and automated quality control methodology for radiography and mammography. **Journal of Applied Clinical Medical Physics**, Louisville, vol 22, p. 1–17, 2021.
- [10] FITTON, I. *et al.* Two-Dimensional Mammography Imaging Techniques for Screening Women with Silicone Breast Implants: A Pilot Phantom Study. **Bioengineering**, v. 11, n. 9, p. 884–884, 31 ago. 2024.

- [11] DRTECH Co, Ltd. “RSM1824C / RSM2430C User Manual”. Disponível em: <https://www.drtech.co.kr/kr/>. Acesso em: 30 dez. 2024.
- [12] KODAK. DIAGNOSTICS for the Kodak DirectView CR 825/850 SYSTEMS Service Codes: 5634, 4825. Manual, 2005.
- [13] SIEMENS. Mammography Applications for MAMMOMAT 1000/3000 Nova. Manualslib, 2004. Disponível em: <https://www.manualslib.com/download/1605263/Siemens-Mammomat-1000Nova.html>. Acesso em: 30 dez. 2024.
- [14] EFOMP - European Federation of Organizations for Medical Physics. EFOMP Mammo Protocol. Quality controls in Digital Mammography. 2017.
- [15] ALMEIDA, L. F. M. *et al.* Intercomparison of modulation transfer function in mammography using quality control softwares. In: **Semana nacional de engenharia nuclear e da energia e ciências das radiações**. Anais. Belo Horizonte (MG) UFMG, 2024. Disponível em: <https://www.even3.com.br/anais/vii-sencir-semana-nacional-de-engenharia-nuclear-e-da-energia-e-ciencias-das-radiacoes-449507/903883-INTERCOMPARISON-OF-MODULATION-TRANSFER-FUNCTION-IN-MAMMOGRAPHY-USING-QUALITY-CONTROL-SOFTWARES>. Acesso em: 30 dez. 2024.
- [16] ALMEIDA, L. F. M. *et al.* Comparative evaluation of materials for measuring the modulation transfer function in an amorphous silicon detector for digital mammography. ISSSD 2024: 24 international symposium on solid state dosimetry, Mexico: Sociedad Mexicana de Irradiacion y Dosimetria. **INIS-IAEA**, 2024.
- [17] MINITAB. Minitab Statistical Software, versão 18 [software]. State College, PA: Minitab, Inc., 2017.

---

## LICENSE

This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The images or other third-party material in this article are included in the article's Creative Commons license, unless indicated otherwise in a credit line to the material. To view a copy of this license, visit <http://creativecommons.org/licenses/by/4.0/>.