Simulation of breast lesions based upon fractal Perlin noise

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\section*{1. Introduction}

Demands for more personalized breast cancer diagnostics are constantly increasing, and the optimization and evaluation of modern imaging systems require matching technical development \cite{1,2}. In the context of breast imaging, the ultimate evaluation of a system would be described in terms of sensitivity and specificity for a given clinical detection task, or the observed range of values for a given quantitative characterization task. Clinical imaging trials, therefore, remain the overall ideal method for evaluating the clinical performance of an imaging system. However, conducting clinical trials is highly resource-demanding, with known limitations in terms of high costs with respect to time and money, the available volunteer subjects and potential health risks, e.g., when using ionizing radiation. These limitations make clinical imaging trials unsuitable for addressing evaluation and optimization tasks during the development of modern medical imaging systems.

The gold standard for analyzing the performance of imaging systems is the use of technical or anthropomorphic physical phantoms. Technical phantoms (like the CD-MAM phantom) can be sufficient for specific systematic performance tasks, such as, e.g., continuous surveillance of the status of imaging devices by calculating physical figures of merit. However, the translation between these figures of merit to clinical performance remains unclear \cite{3}. Anthropomorphic phantoms resemble human anatomy and are commonly used for evaluating e.g. new imaging protocols and rely on observers for evaluation of image quality. However, their anatomical background lacks variation which limits their ability to represent clinical patient populations.

Virtual clinical trials (VCTs), sometimes referred to as in silico trials, are a fast-growing specialty for preclinical (and/or co-clinical) validation of medical imaging systems \cite{4,5}. VCTs have emerged as an...
affordable alternative to clinical imaging trials in various evaluation tasks, as they primarily rely on computer-generated data. In a recent review by Abadi et al., a detailed description of the basic principles and various applications of VCTs in medical imaging has been summarized [4]. The acceptance of computational/virtual phantoms as an appropriate tool for evaluating breast imaging systems is related to the level of realism in the computer representation of breast anatomy. This is even more emphasized for the computer models of breast lesions [6-8], due to their wide morphological and functional variability and complexity as seen in clinical practice. Despite the recent progress in improving the realism of simulated lesions, the models are still in need of refinement and improvement [9]. Moreover, the validation against clinical lesions needs to be studied to a greater extent to be able to produce virtual structures and shapes that resemble the clinical variations [9].

The analysis and validation of virtual lesions can aid us in better understanding the lesion complexity. One could consider that the future of lesion assessment should not only rely on qualitative and visual appearance but also on quantitative assessment of lesion shape, which could be adequately studied by assessing virtual lesions. The use of mathematical and analytic approaches to describe the lesion shape and margin is gaining increased popularity; especially as deep learning is rapidly playing a larger role in breast cancer diagnostics. These neural networks are trained to localize and characterize lesions in mammographic images based on radiographic features, also known as radiomic features, which can be related to the mathematical description of lesion shape and margins [10]. When generating the clinical variation of breast lesions, we also need to understand how the shape descriptors are related to the clinical characterization of the lesion.

In this work, we simulated soft tissue breast lesions with a novel method based upon fractal Perlin noise. Perlin noise is a pseudo-random function used to generate gradient noise structures [11]. It has been widely used in computer-generated imagery, based upon the notable ability to generate realistic structures and textures, e.g., clouds, mountains, landscapes; human and animal skin; optical reflectance of various natural surfaces, etc. [11]. A more complex form of Perlin noise is fractal Perlin noise, where structures of a range of discreet frequencies are separately generated and combined. This allows for a more complex and nuanced structure. Our lab has previously demonstrated the use of fractal Perlin noise in modelling normal human breast tissue [12,13]. In this paper, we are expanding the previous work in order to also simulate breast lesions.

The properties and computational feasibility of fractal Perlin noise motivate its use in simulating breast lesions for simulated medical imaging. This approach allows more user control in a systematic simulation of the clinical appearance of breast anatomy and abnormalities. To assess the clinical plausibility of the simulated lesions we need to relate their appearance to clinical lesions. Clinically, mammographic findings are categorized based upon the established BI-RADS assessment (categories 0-6, where zero corresponds to incomplete evaluation and six to previous biopsy-proven malignancy) [14].

The aim of this study was to demonstrate the use of Perlin noise for generating computer-simulated soft tissue breast lesions. We intended to simulate the radiographic variation of breast lesions as described by the BI-RADS assessment criteria. We have characterized simulated lesions using both quantitative and qualitative approaches.

2. Method and materials

2.1. Lesion generation

Our lesion model consisted of a solid 3D shape (spherical or ellipsoidal preliminary, though other, user-designed shapes may be allowed) of a certain, assigned size. We used our Perlin noise algorithm from our previous work on simulated breast tissue [12,13]. In short, a Perlin noise function is evaluated at each voxel coordinate in a 3D space. This is repeated for several successive octaves and the results are combined into a fractal Perlin volume. Each octave is Perlin noise generated with one discrete frequency. We have used either spherical or ellipsoidal base shapes, to resemble either round or oval lesions. We have then iteratively adjusted the number of octaves used and the amplitude of the specific octaves, to generate different lesion shapes. These parameters were varied until a desirable lesion shape was obtained. To investigate the overall major alterations in shape, we only used a limited number of frequency combinations. The majority of the lesions were simulated using only two octaves of different frequencies and the maximum number of octaves was four. The octaves had frequencies 1, 2, 4, 8 and 16 (noise cycles per axis). Round and circumscribed lesions were generated by intensifying the low frequencies (i.e., increasing their amplitude). Irregular and microlobulated lesions were generated by intensifying the high frequencies. To simulate obscured and indistinct margins, the location of the lesion within the breast phantom was selected in regions containing a higher proportion of simulated parenchymal structures. We did not simulate spiculated lesions, the focus was to only simulate non-spiculated soft tissue lesions.

2.2. Breast phantom outline and the simulation of radiographic image acquisition

We used the method developed by Rodriguez et al. to model the breast phantom outline [15,16]. The breast tissue was simulated using our Perlin noise algorithm [12,13]. The phantom and lesions had a voxel size of 0.2 mm. Radiographic projections of the phantom were generated by the open-source software OpenVCT, which is used for simulating mammographic and tomosynthesis image acquisition [17]. The voxel values of the simulated breast phantoms and lesions were assigned specific materials representing different tissue types according to the OpenVCT material library. The different tissue types were set to a mix between adipose and glandular tissue. The exact proportions (or weighted values) are seen in Table 1. Voxel values zero and six are assigned for air and skin, respectively. Voxel value seven is assigned for the lesion.

The current lesion composition, i.e. the weighted value of glandular tissue (0.86, seen in Table 1), was selected interactively, with the help of a breast radiologist, to match the simulated lesion conspicuity with clinical lesions. The radiographic projections were simulated based upon the Siddon raytracing algorithm [17], assuming the acquisition geometry of a Siemens Mammatom Inspiration (Siemens Healthineers, Forchheim, Germany) digital mammography (DM) system. All projections were acquired in mediolateral view (ML). The pixel size of the projected images was 0.085 × 0.085 mm. The raw projections were post-processed by using a Siemens Mammatom Inspiration unit available at our clinic. All simulations were performed on a Microsoft Windows 10 Pro PC, with an AMD Ryzen Threadripper 2970WX 24-Core Processor and an NVIDIA GeForce RTX 2080 Ti GPU.

2.3. Quantitative characterization of simulated lesions

We have calculated the aspect ratio (AR), sphericity and convex deficiency of the simulated lesions. The AR is defined as the ratio between the longest axis and the shortest axis, to indicate how elongated or flattened the lesion is. Sphericity is the ratio between the volume of the lesion and the volume of a nominal sphere that has the same surface area as the lesion. Sphericity characterizes the irregularity of the lesion. A perfect sphere will have a sphericity value of one. Convex deficiency is the ratio between the volume of the lesion and the volume of the smallest possible convex hull around the lesion. We used the binary output of the simulated lesions, i.e. the three-dimensional lesion mask, to calculate AR, sphericity and convex deficiency. The volume of each lesion and the length of the principal axis in each dimension (x, y and z) were calculated voxel-by-voxel of the binary lesion output. We calculated the average time it takes to simulate 30 lesions and the corresponding standard deviation. We also investigated the computational...
Table 1
The tissue types used in OpenVCT for each voxel value of the Perlin phantom, including the lesion. Each tissue was set to be a combination of adipose and glandular tissue, the proportions (or the weighted values) are shown in the table. The lesion was set to only contain glandular tissue with a weighted value of 0.86.

<table>
<thead>
<tr>
<th>Voxel value</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Material</td>
<td>Air</td>
<td>Breast tissue</td>
<td>Breast tissue</td>
<td>Breast tissue</td>
<td>Breast tissue</td>
<td>Breast tissue</td>
<td>Skin</td>
<td>Lesion</td>
</tr>
<tr>
<td>The proportion of adipose/glandular tissue</td>
<td>N.A.</td>
<td>1.00/0.00</td>
<td>0.9/0.1</td>
<td>0.8/0.2</td>
<td>0.7/0.3</td>
<td>0.6/0.4</td>
<td>N.A.</td>
<td>0.00/0.86</td>
</tr>
</tbody>
</table>

Fig. 1. Illustration of a lesion scored high in realism and categorized as round and obscured by the observer. Shown is the lesion in: (a) parallel projection without background tissue, (b) a slice through the phantom with the inserted lesion, and (c) a simulated DM of the phantom with the inserted lesion, indicated by the arrow.
memory load while simulating the lesions. All calculations were performed in Matlab 2021b (MathWorks Inc., Natick, MA, USA).

2.4. Qualitative review of simulated lesions

Three radiologists participated in observer experiments with simulated lesion images, a breast radiologist, a radiology specialist and a radiology resident (approximately six years, one year and one month of self-reported experience, respectively, with reading mammograms). They reviewed images of 30 simulated Perlin lesions. Images were presented on clinical displays (Radiforce, RX660, EIZO, Japan). The study was set up in the open-source software ViewDEX 3.0 [18–21]. The observers were asked to classify the lesions according to the shape, margin and density categories used in the BI-RADS assessment criteria for soft tissue lesions [14]. The risk of malignancy for soft tissue lesions is assessed based upon their appearance in images: size, shape (oval, 

![Fig. 2. Illustration of a lesion scored high by the observer in shape-, margin- and overall realism. Shown is the lesion in: (a) parallel projection without background tissue, (b) a slice through the phantom with the inserted lesion, and (c) a simulated DM of the phantom with the inserted lesion, indicated by the arrow.](image-url)
round, or irregular), margin (circumscribed, obscured, microlobulated, indistinct, spiculated) and density (high, equal, or low, relative to the background tissue). Generally, irregular, spiculated and high-density lesions have a higher risk of being malignant. They also rated (scale of 1–5) how well the shape and margin resembled clinical lesions (1 = poor, 2 = fair, 3 = moderate, 4 = good, 5 = excellent). Lastly, we asked the observers to give an overall rating of the realism of the simulated lesion (scale of 1–5).

2.5. Evaluation and statistics

Analysis and statistics were performed in Matlab 2021b and R version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria). The mean and standard deviation of the geometrical properties (volume, AR, sphericity, convex deficiency) were calculated. We calculated the average score (scale of 1 to 5) for each assessed lesion by combining the ratings provided by the observers. For the BI-RADS categories, we applied the mode measure, meaning that we decided on the shape and margin by selecting according to the majority. Cases with no majority were excluded from further analysis.

Fig. 3. A lesion that was considered by the observers to have low levels of realism. Shown is the lesion in: (a) parallel projection without background tissue, (b) a slice through the phantom with the inserted lesion, and (c) a simulated DM of the phantom with the inserted lesion, indicated by the arrow.
We compared the overall realism score with the shape and margin categories to identify which category the observers found most realistic. Categories that were assigned less than five lesions were excluded from any statistical tests. The statistical test used to compare the categories was nonparametric (Mann-Whitney U test).

3. Results

3.1. Simulated lesions and virtual DM images

Figs. 1–3 showcase a selection of the simulated phantoms and lesions, and their corresponding virtual projection. The cases represent three examples that include both lesions that received high and low scores from the observers, related to the realism of their shape and margin. The images of example lesions are followed by their quantitative characterization (Tables 2 and 3).

The lesion shown in Fig. 1 was scored high by all observers when assessing the shape (average score 5 out of 5) and margin (average score 4 out of 5). The longest diameter axis of the lesion was 8 mm. Observers categorized the lesion as round and obscured. This lesion was simulated using only two frequencies (octaves 1 and 2). The first octave had an amplitude value of 4 and the second octave had an amplitude value of 1. AR, sphericity and convex deficiency were close to one (0.84, 0.99, 0.98, respectively).

Fig. 2 illustrates a lesion that received an average score of 4 in shape-, margin-, and overall realism. The observers classified the lesion as oval and microlobulated. The longest diameter axis of the lesion was 12 mm. AR, sphericity and convex deficiency were 0.70, 0.79 and 0.87, respectively. To generate the lesion, we used three different frequencies (octaves 1, 2 and 4). The amplitude was higher for octaves 2 and 4 (amplitude value 3) compared to octave 1 (amplitude value 0.02).

The lesion in Fig. 3 demonstrates a lesion that received an overall low score from the observers (2 out of 5 both for shape-, margin- and overall realism). The lesion was categorized as oval and circumscribed and was 13 mm in diameter (the largest principal axis length). We used the first and second octaves to simulate this lesion and we used the same amplitude (amplitude value 4) for both. AR, sphericity, and convex deficiency were 0.64, 0.94 and 0.98, respectively.

3.2. Quantitative characterization of simulated lesions

The quantitative characterization of the lesions is reported in Tables 2 and 3. In Table 2 we present the mean size of the lesion, as the mean principal axis length in all dimensions (x, y and z). The lesion size is within the range of clinically representative lesions.

In Table 3 we report the mean lesion volume, together with the quantities related to defining the shape and margin: AR, sphericity and convex deficiency, as defined in Section 2.3. Presented is the mean value for all 30 lesions, as well as the corresponding standard deviation.

The average computational time (averaged over all 30 simulated cases), and the corresponding standard deviation, for generating one Perlin noise lesion was 1.4 ± 1.0 s. The computational memory used while simulating lesions ranged between 140 and 210 MB. Note that this is not the final computational time or computational memory for generating breast phantoms, projecting and processing the virtual images.

3.3. Qualitative review of simulated lesions

The observers’ combined characterization of the simulated lesions, according to BI-RADS, is shown in Fig. 4. Four cases were excluded in the shape analysis (Fig. 4b) due to no agreement between the observers (no majority), respectively two cases in the margin analysis (Fig. 4b). The spiculated category was offered to the observers for completeness, however, no lesions were simulated with ground true spiculated margin (Fig. 4b).

We also found that the lesions that received a fair level of overall realism (score 2 out of 5) were all classified as oval and circumscribed, excluding one case where there was no agreement between the observers with regard to which shape category the lesion belonged to. No oval lesion received a higher overall realism score above 2.

The lesion density, as perceived by the observers, is shown in Fig. 6. The majority of the lesions were considered to be radiographically denser than the tissue background.

3.4. Overall realism score compared to lesion shape and margin

The lesions that were classified as round received significantly higher overall realism scores (p = 0.02) compared to the oval lesions (Fig. 7a). We could not prove the same for irregular lesions due to too few cases. Lesions that were classified as obscured, microlobulated or indistinct received a higher overall realism score, compared to circumscribed lesions. Due to too few obscured and indistinct lesions, we could not make a comparison between all four margin categories. However, we did find that lesions that were categorized as having a microlobulated margin received significantly higher overall realism scores (p = 0.02) compared to circumscribed lesions (Fig. 7b).

4. Discussion

In this study, we developed an algorithm for generating simulated soft tissue breast lesions based on fractal Perlin noise. Our initial validation of the lesion appearance was restricted to a subset of parameters of the modelling algorithm, selected to match lesion characteristics as described by BI-RADS assessment criteria [14]. In a qualitative assessment, three observers evaluated the shape, margin and density of simulated lesions. We showed that our algorithm can produce a variation in both shape and margin, according to BI-RADS (Fig. 4a and b), with a moderate/well level of realism (Fig. 5). Our simulated lesions varied in size, within the size range of clinically representative breast lesion masses (5–20 mm) as shown in Table 2. The simulated lesions were mainly perceived as being denser than the surrounding tissue, which may be more representative of clinically malignant cases (Fig. 6). However, if needed it is possible to change the material properties of the lesion to alter its relative density.

Moreover, we compared the overall realism score to the shape and margin to evaluate which lesions were considered realistic. We were able to show that oval and circumscribed lesions received a lower overall realism score compared to round and microlobulated lesions (Fig. 7). All lesions that were scored with a low level of overall realism (score 2 out of 5) were oval and circumscribed. In this study, we simulated lesions of different shapes based on the BI-RADS assessment.

Table 3

<table>
<thead>
<tr>
<th>Mean lesion volume ± standard dev. (mm³)</th>
<th>Mean AR ± standard dev.</th>
<th>Mean sphericity ± standard dev.</th>
<th>Mean convex deficiency ± standard dev.</th>
</tr>
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<tbody>
<tr>
<td>89 ± 40</td>
<td>0.7 ± 0.2</td>
<td>0.8 ± 0.1</td>
<td>0.89 ± 0.1</td>
</tr>
</tbody>
</table>
criteria (round, oval, irregular and with circumscribed, microlobulated, obscured or indistinct margins). However, the results suggest that oval shapes in combination with circumscribed margins should be less prominent in future optimizations of the lesion model as they were scored as less realistic. The lesion in Fig. 3 is an example of an oval and circumscribed lesion that received low overall realism. According to one of the observers (the breast radiologist), the main cause for the low score was the orientation of the lesion. This may be related to the reported observations that breast structures are predominantly oriented towards the nipple [22]. To comprehensively evaluate the impact of combined characteristics (lesion and margin) on overall realism, a larger dataset would be essential to conduct a more detailed analysis.

Further on, we assessed the realism of the shape and margin to get an indication of which lesions (and corresponding simulation parameters) have greater importance in further optimization studies (Fig. 5). It is important to not neglect the impact of the background tissue when assessing the lesion realism. The tissue composition has an equal, if not higher impact on both the realism and the visual interpretation of the lesions. In this study, we did not further stratify the simulated lesions based on if the lesions were placed in simulated adipose tissue or in regions containing more parenchymal tissue. Therefore, the realism score in this study should not necessarily be compared with real lesions, rather it should serve as a first recommendation of suitable lesions for

Fig. 4. The diagrams show how the simulated lesions were characterized by the observers, according to the BI-RADS scale. Diagram (a) illustrates the distribution of the shape characteristics. Diagram (b) illustrates the distribution of the margin characteristics. The majority of the simulated lesions were characterized as oval (or round), with circumscribed margins. All types of lesion characteristics, except spiculated lesions, were represented in our subset of simulated lesions.

Fig. 5. The distribution in shape realism (a), margin realism (b) and overall lesion realism (c). Observers ranked the lesion realism between; poor, fair, moderate, well, excellent or not applicable. The majority of the simulated lesions were considered to have a realism score of moderate to well.

Fig. 6. The lesion density as perceived by the observers. The majority of lesions were considered to have a higher density than the tissue background.
further assessment or further use. However, cases that were characterized as having obscured, or indistinct margins were receiving higher overall realism scores. This could indicate that the observers were influenced by the location of the lesion. As part of future work, we consider measuring parenchymal descriptors at the lesion insertion site, to optimize the insertion.

This is the first attempt to study the Perlin noise and its relation to radiographic lesion characteristics. In an initial quantitative assessment, we selected basic descriptors of lesion shape and margin (Table 3). We focused on a certain set of noise frequencies to study the effect on the shape, margin and perceived realism. Further studies are necessary to understand the complex relationship between Perlin noise parameters and quantitative descriptors (such as AR, sphericity and convex deficiency), as well as their relation to perceived realism.

When it comes to computational capacity, the Perlin-generated lesions can be simulated near real-time. This is of practical interest, as the simulation time is a crucial aspect, which may limit VCT performance. Moreover, the proposed Perlin noise-based approach does not require interactive manual segmentation of lesions by the user, making the simulation method efficient and robust compared to other models that rely on clinical patient data [9]. As such, Perlin noise exhibits the level of randomness needed to plausibly represent a broad range of clinically seen breast lesions. Previous mathematical lesion models that have used simple geometric shapes or Gaussian noise to simulate soft tissue lesions do not have this level of randomness, resulting in less realistic lesion appearances [9]. A noted limitation of the proposed model is the lack of spiculated lesions; a modification of the Perlin noise approach to represent spicules is ongoing. Similarly, we are working on the extension of the current approach to simulate growing lesions, based upon our previous methods [23]. As for now, the lesions generated in the current study represented only non-spiculated masses. Our current lesion model assumes a uniform tissue composition of the lesion interior. Internal structures could be added to simulate tissue heterogeneity. This would allow us to represent tumour biology, as related to clinical categorization and risk of malignancy.

Future optimization and evaluation of the lesion model will include a more detailed and systematic assessment based upon a wider set of parameters and quantitative descriptors. AI methods could potentially be used to optimally select parameters of simulated lesions as related to different BI-RADS or clinical categories.

Fig. 7. Comparison between the round and oval lesions (a) showed that round lesions received significantly higher overall realism scores (p < 0.05) compared to oval lesions. Microlobulated lesions received a significantly higher realism score (p < 0.05) compared to circumscribed lesions (b). Lesions that were classified as irregular and/or with obscured and indistinct margins were excluded from the analysis due to too few cases.

5. Conclusion

We presented a novel algorithm for computer simulation of soft tissue breast lesions using Perlin noise. The algorithm enables efficient simulation of lesions, with different sizes and appearances.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References


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