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Effect and correction of optode coupling errors in breast imaging using diffuse optical tomography

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Abstract: In diffuse optical tomography (DOT) and spectroscopy (DOS) using handheld probes, tissue curvature can cause bad fiber-to-tissue contact. Understanding and minimizing image artifacts caused by these coupling errors would significantly improve DOT and DOS image quality. In this work, we utilized Monte Carlo simulations and experiments with gelatin-Intralipid phantoms to systematically study the influence of source or detector (optode) coupling errors. Optode coupling errors can increase the amplitude and decrease the phase of the measured diffuse reflectance, creating artifacts in the reconstructed absorption maps, such as hot spots on the edges. We propose an outlier removal algorithm that can correct these image artifacts, and we demonstrate its performance using simulations, phantom experiments, and breast patient data acquired with bad probe contact due to a dense or small breast. Further, we designed and implemented a new resistance-type thin-film force sensor array that provides real-time optode coupling feedback and guides the outlier removal to minimize optode coupling errors. Our approaches and study results have significant implications for reducing image artifacts arising from handheld probes, which are commonly used with mobile and wearable DOT and DOS devices.

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1. Introduction

Near-infrared diffuse optical tomography (DOT) has demonstrated its potential in distinguishing benign from malignant breast lesions and in monitoring breast cancer neoadjuvant chemotherapy response [1–5]. However, DOT image reconstruction is an ill-posed and ill-conditioned inverse problem, and suffers from uncertainty in the reconstructed target location and target quantification [6]. Ultrasound (US)-guided DOT utilizes co-registered real-time ultrasound to provide a lesion’s morphology and location to the DOT imaging reconstruction algorithm and to improve the accuracy of the reconstructed optical properties of the lesion [7–11]. In addition to breast imaging, US-guided DOT has found many clinical applications in maternal health and thyroid cancer [12,13].

DOT image reconstruction can be affected by model errors when the experimental conditions do not match the assumptions made in the forward model [14]. To reduce the mismatch between the forward model and experimental data, the measured diffuse reflectance from the lesion (target) side breast can be normalized to the contralateral normal breast (the reference side) to reconstruct the lesion optical absorption map [15]. This “normalized perturbation” is calculated by subtracting the reference side measurements from the lesion side measurements, then dividing
the result by the reference side measurements. However, imaging artifacts can still appear due to mismatches between the two sides in tissue curvature, tissue heterogeneity, the depth and angle of the chest wall underneath the breast tissue, and source or detector (optode) coupling. During patient studies, these errors can all cause misinterpretation of lesion images. Our group has extensively studied lesion reconstruction problems caused by chest wall mismatch between the lesion side and the reference side [16–18].

Many DOT and diffuse optical spectroscopy (DOS) implementations involve a fiber-optic-based probe that is pressed against the tissue to deliver light and collect diffuse reflectance [13,19–24]. However, the curvature of the imaged tissue can cause fiber-to-tissue contact problems, affecting the light coupling in both directions and introducing inaccuracy in measurements of the tissue’s optical properties. Understanding and characterizing the effects of optode coupling problems on DOT images is important to avoid potential errors during data acquisition and to identify image artifacts in reconstructed images. Several research groups have investigated optode coupling problems and simulated the errors as contaminated measurements by manually allocating coupling coefficients to the intensities and/or the phases of the sources and detectors [25–28]. Coupling errors were experimentally created by utilizing hairs to block the light or by pulling back the optical fibers [26,27]. Nevertheless, optode coupling errors caused by air gaps in practical experimental situations remain uninvestigated. Furthermore, the reported studies focused on correcting optode coupling errors after data contamination, but it is more desirable to avoid coupling errors during data acquisition. Mastanduno et al. developed an adjustable triangular breast interface for their MRI-guided DOT system, where the fibers could be adjusted in six degrees of freedom to improve their contact with multiple sizes of breasts [29]. Gulser et al. utilized a pressure sensor for each fiber probe in a hybrid MRI-DOT system to ensure good contact after the fibers were pushed against the breast by hydraulic actuators [30]. Both approaches were time-consuming on adjusting the fiber contact with the breast. Cerussi et al. integrated one force sensor into their DOS handheld probe and found the variations in small contact force did not significantly influence the measured breast tissue optical properties [31].

Here, we use Monte Carlo simulation and experiments on phantoms to systemically study the effects of probe-to-tissue coupling, which is often encountered in clinical studies using a hand-held probe. Different optode coupling mismatch conditions are investigated, as well as different target sizes, depths, and contrasts. An outlier removal algorithm and a new force sensor array are introduced to reduce image artifacts caused by optode coupling mismatch. Examples of patient data illustrate the effects of optode coupling errors on image quality, demonstrate the improvement achieved by the outlier removal algorithm, and suggest the potential benefit of real-time contact feedback from the force sensor array.

2. Methods

2.1. US-guided DOT system

All simulations and phantom studies were performed using the compact, frequency domain US-guided DOT system described in Ref. [24]. Briefly, four wavelengths -730, 785, 808, and 830 nm – were sequentially switched to the nine source positions on the probe, shown in Fig. 1. Fourteen light guides of 3 mm diameter couple the light reflected from the tissue to 14 photomultiplier tubes (PMT). A customized A/D board with a 200 Hz sampling rate and 18-bit resolution digitized the detected signals and stored the data in a PC. All phantom experiments were conducted at 785 nm. Other wavelengths gave similar conclusions. For patient studies, all wavelengths were used to calculate the total hemoglobin (tHb) distribution. For co-registered imaging, a US transducer is inserted into the middle of the DOT probe, as seen in Fig. 1(b). It acquires B-scan images of the lesion in the x-z plane and provides the lesion size and depth information. The lesion size in the y-direction is assumed to be the same as in the x-direction. The entire data acquisition time was about 3 seconds.
Fig. 1. (a) Handheld US-DOT probe with thin-film force sensors. (b) US probe and force sensor (blue circles) locations with respect to the probe.

Fig. 2. (a) Illustration of the cross-section of the tissue volume used in Monte Carlo simulation. (b) The top plane (cropped to 15 cm × 15 cm for better visualization) and y-z cross-sections of the tissue with respect to the probe, with and without optode coupling errors. Left: the tissue is in the original position. Middle: the tissue is moved 1.25 cm in the -y direction. Right: the tissue is moved 1.75 cm in the +y direction.
2.2. Monte Carlo optode coupling mismatch models

A hemispherical shape with a 7.5 cm radius was designed and cropped to mimic a curved breast compressed by a DOT handheld probe during clinical studies. For Monte Carlo simulation [32], the volume surrounding the compressed hemisphere was filled with air, achieving a total volume of $20 \text{ cm} \times 20 \text{ cm} \times 6 \text{ cm}$, with a grid size of $0.25 \text{ cm} \times 0.25 \text{ cm} \times 0.25 \text{ cm}$. The cross-section of the volume and its dimensions are shown in Fig. 2(a). The incident light was modeled as a pencil beam. The detectors were modeled as voxels over the described $20 \text{ cm} \times 20 \text{ cm} \times 6 \text{ cm}$ volume, and photons that passed through the virtual detector voxel bottom surface were collected.

To simulate bad optode coupling conditions that are likely to happen in clinical breast imaging using the described DOT configuration, the hemispherical tissue was moved 1.25 cm in the -y direction or 1.75 cm in the +y direction, while the probe remained fixed. The simulated top planes of the compressed tissue with respect to the optode positions, with and without optode coupling errors, are shown in Fig. 2(b). The background optical absorption coefficient ($\mu_a$) was set to 0.02 cm$^{-1}$ and the reduced scattering coefficient ($\mu_s'$) was set to 7 cm$^{-1}$, which represent the average breast tissue optical properties [33]. For air, $\mu_a = 0$ and $\mu_s' = 0$. To perform the forward calculation for the lesion side, a spherical target was inserted below the center of the DOT probe. Targets with different sizes, depths, and contrasts were utilized to represent different types of lesions. For the high contrast targets, $\mu_a = 0.2 \text{ cm}^{-1}$ and $\mu_s' = 7 \text{ cm}^{-1}$; for the low contrast targets, $\mu_a = 0.1 \text{ cm}^{-1}$ and $\mu_s' = 7 \text{ cm}^{-1}$, unless otherwise noted. The refractive indexes of the air, background tissue, and targets were set to 1, 1.33 and 1.33, respectively, and the reflection at air-tissue boundaries was calculated based on Fresnel’s law [32].

2.3. Phantom and patient experiments

2.3.1. Tissue-mimicking phantom preparation

Hemispherical phantoms (Fig. 3) with or without silicone targets were fabricated and used as the target side and the reference side, respectively. The surrounding background material was made of ultra-purified deionized water, Intralipid 20% IV fat emulsion (2B6022, Baxter International Inc., Deerfield, IL) diluted to 1%, and 5% Type A 300 Bloom gelatin derived from acid-cured porcine skin (G2500, Sigma-Aldrich Corp., St. Louis, MO), following the procedures in Ref. [34]. The calibrated background optical properties at 785 nm were $\mu_a \approx 0.02 \text{ cm}^{-1}$ and $\mu_s' \approx 6.1 \text{ cm}^{-1}$, measured using the DOT fitting procedure described in Ref. [35]. The silicone target had $\mu_a \sim 0.23 \text{ cm}^{-1}$ and $\mu_s' \sim 7.0 \text{ cm}^{-1}$.

![Fig. 3. Intralipid and gelatin-based hemispherical phantom.](image)

2.3.2. Force sensor array for monitoring optode coupling in real time

The described hemispherical phantoms were used to emulate clinical studies, and a resistance-type thin-film force sensor array was designed to monitor the contact between the phantoms and the probe in real-time. Eight force-sensing resistors (Interlink Electronics FSR 400 Series) were placed on the probe plane near the sources and detectors on the edge (Fig. 1). A voltage
divider and the A/D converter function of the microcontroller (MSP430F5529) were used to calculate the resistance of the force sensors. The force value was then determined from the resistance-force curve of the sensors. The data set was transported back to the computer in Universal Asynchronous Receiver/Transmit (UART) mode, with the positions flagged so that the force value could be displayed directly by a MATLAB graphical user interface (GUI) with corresponding positional information. A threshold value for the force level could be adjusted to use eight indicators to display whether the force level was above the threshold (good contact) or not (bad contact). This procedure ensured that in good coupling conditions, the optode made solid contact with the tissue. In the experiments, we ensured all force sensors on the target side were in good contact, and we adjusted the probe positions on the reference side to create bad contact conditions. After data acquisition, to correct coupling errors, we removed measurements from edge optodes between two force sensors that had force levels below the threshold.

2.3.3. Patient examples

The described US-guided DOT system was used for clinical studies. The study protocol was approved by the local Institutional Review Board and was compliant with the Health Insurance Portability and Accountability Act. Data from two patients with dense or small breasts that had bad probe-tissue contact during data acquisition were used to illustrate the effects of optode coupling errors and evaluate the outlier removal algorithm. Based on extinction coefficients obtained from Ref. [36], the hHb distribution was computed by linear weighting of the absorption maps of all four wavelengths.

2.4. Reconstruction, outlier removal algorithms, and quantification of image artifacts

DOT data acquisition was performed on both the target side and the contralateral reference side. For our frequency-domain DOT system, the normalized perturbation for each source-detector pair \( U_{sc}(i) \) was calculated as

\[
U_{sc}(i) = \frac{A_f(i)e^{i\phi_f(i)} - A_r(i)e^{i\phi_r(i)}}{A_r(i)e^{i\phi_r(i)}} \left( \frac{A_f(i)}{A_r(i)} \cos(\varphi_f(i) - \varphi_r(i)) - 1 \right) + j \frac{A_f(i)}{A_r(i)} \sin(\varphi_f(i) - \varphi_r(i)),
\]

where \( A_f(i) \), \( A_r(i) \), \( \varphi_f(i) \), and \( \varphi_r(i) \) are the measured lesion side amplitude, reference side amplitude, lesion side phase, and reference side phase corresponding to the source-detector pair \( i \). Our DOT inverse problem was linearized by Born approximation, and was formulated as the following regularized optimization problem:

\[
f(x) = \arg \min_{\delta \mu_a} \left( \| U_{sc} - W \delta \mu_a \|^2 + \frac{\lambda}{2} \| \delta \mu_a \|^2 \right).
\]

Here, \( \delta \mu_a \) represents the unknown changes of optical properties, \( W \) is a sensitivity matrix in the semi-infinite homogenous medium that describes the measurement’s sensitivity to changes in optical properties, and \( \lambda \) is a regularization parameter. A conjugate gradient (CG) algorithm was employed to solve \( \delta \mu_a \), using a dual-mesh scheme [37]. Briefly, the entire tissue was segmented into a lesion region (fine-mesh area with voxel size \( 0.25 \times 0.25 \times 0.5 \) cm\(^3\)), and a background region (course-mesh area with voxel size \( 1.5 \times 1.5 \times 1.5 \) cm\(^3\)). The reconstructed volumetric absorption map contains seven layers in the depth- or z-direction, with a 0.5-cm spacing between two adjacent layers. In DOT reflection geometry, the majority of the photons are absorbed by the upper part of a highly absorbing lesion, and fewer photons reach the lower portion of the lesion and get detected by the detectors. Thus, the lower part of the lesion is under-reconstructed [38]. For better visualization in simulation and phantom experiments, we present only the top layer of the reconstructed image containing the target.
An outlier removal algorithm was applied when there was an optode coupling mismatch. This algorithm removed the measurements from optode(s) that had large model errors, i.e., where the difference between the original perturbation $U_{sc}$ and the projected perturbation $W\delta\mu_a$ was larger than the threshold set in the first step of the algorithm, as detailed below. All image reconstruction and outlier removal were conducted using MATLAB.

Algorithm 1. Outlier removal algorithm for optode coupling mismatch errors

<table>
<thead>
<tr>
<th>Input:</th>
<th>Original normalized perturbation $U_{sc}$, weight matrix $W$, regularization parameter $\lambda$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Reconstruct the original absorption map $\delta\mu_a_{\text{orig}}$ using $U_{sc}$ according to equation (2). If the objective function $|U_{sc} - W\delta\mu_{a_{\text{orig}}}|^2 + \frac{1}{2}|\delta\mu_{a_{\text{orig}}}|^2 &gt; \text{threshold}$, perform the following outlier removal. Here, threshold $= 0.2$ was empirically chosen based on our observations in simulation and phantom experiments that the objective functions of cases with / without coupling errors are typically larger / smaller than 0.2, respectively.</td>
</tr>
<tr>
<td>2.</td>
<td>Calculate the pointwise difference $\text{Diff}$ between the original perturbation, $U_{sc}$, and the projected perturbation, $W\delta\mu_{a_{\text{orig}}}$: $\text{Diff} = U_{sc} - W\delta\mu_{a_{\text{orig}}}$</td>
</tr>
<tr>
<td>3.</td>
<td>If a point $j$ in $\text{Diff}$ satisfies $\text{abs}(\text{Diff}(j)) &gt; C \times \text{median}(</td>
</tr>
<tr>
<td>4.</td>
<td>For any source or detector, if the number of outliers is more than 1/3 of all points corresponding to that optode, remove all perturbation and weights corresponding to that optode.</td>
</tr>
<tr>
<td>5.</td>
<td>Reconstruct $\delta\mu_{a_{\text{new}}}$, using the new perturbation and weight matrix.</td>
</tr>
</tbody>
</table>

The structural similarity index (SSIM) expresses the similarity of two images in terms of their luminance, contrast, and structure, taking values between 0 and 1. A higher SSIM indicates greater similarity, and an SSIM of 1 means two images are identical. More details on the SSIM can be found in Ref. [15]. In the current study, the reconstructed volumetric absorption maps were used to calculate SSIMs between the match and mismatch conditions to quantify the image artifacts caused by the mismatch. Student’s t-test was used to evaluate the statistical significance after applying the outlier removal algorithm. A p-value of less than 0.05 was considered statistically significant.

3. Results

3.1. Simulation and phantom results

3.1.1. Influence of optode coupling errors

Figure 4 shows $\log(A, p^2)$, where $A_r$ is the amplitude and $p$ is the source-detector distance, and the phase $\phi_s$ of simulated light reflectance on the homogeneous reference side versus the $p$, with and without optode coupling errors. When there are no coupling errors, $\log(A_r, p^2)$ and $\phi_s$ are linearly related to the source-detector distance (Fig. 4(a)), which is consistent with the analytical solution using diffusion theory for a semi-infinite medium [39]. As shown in Fig. 4(b), when source #9 has an air gap, the amplitude corresponding to this source increases (the 14 points circled in red in Fig. 4(b), middle), and the phase corresponding to source #9 decreases (the 14 red points in Fig. 4(b), right). Similarly, in Fig. 4(c), when five detectors have air gaps, 45 measurements have increased amplitudes and decreased phases. Similar findings were also observed in the phantom experiments.

Figure 5 shows representative absorption maps for optode coupling mismatch cases, where similar image artifacts are present for simulation and phantom experiments. When source #9 has an air gap on the target side, indicated by its position outside the perimeter of the simulated compressed breast tissue phantom, the image artifacts at a depth of 1.25 cm appear as two hot
Fig. 4. Simulated $\log(A, \rho^2)$ and $\phi_r$ of light reflectance on the reference side vs. source-detector distance (a) without optode coupling errors, (b) with optode coupling errors on the source side, and (c) with optode coupling errors on the detector side. Red circles indicate measurements from optodes that have air gaps.
spots (enclosed in black circles) close to the two sources near the boundary that do not have an air gap (sources #6 and #8). When the same coupling error happens on the reference side, the hot spot at a depth of 1.25 cm (circled in black) is on the edge of the fine-mesh area of the dual-mesh regime and close to source #9, which has an air gap. When detectors have coupling problems on the target side, no obvious edge artifacts are observed, but the reconstructed target has a distorted shape. When the same error happens on the reference side, hot spots occur on the edge of the fine-mesh area and close to the detectors above the air gap. The above-mentioned image artifacts have similar patterns among different depths, but artifacts’ $\mu_a$ decease at deeper depths. Compared to the cases without coupling errors, the changes in the maximum reconstructed $\mu_a$ due to optode coupling errors are less than 12% for both the simulations and experiments, as shown in Table 1.

| Table 1. Maximum reconstructed absorption coefficient ($\mu_a$) with and without optode coupling errors |
|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
|                               | Simulations                   | Experiments                   |                               |                               |
|                               | Maximum                       | Changes                       | Maximum                       | Changes                       |
|                               | $\mu_a$                       | compared to no coupling error | $\mu_a$                       | compared to no coupling error |
| No optode coupling error      | 0.199                         | -                             | 0.197                         | -                             |
| Source coupling error on the target side | 0.211                         | + 8.0%                        | 0.201                         | + 2.0%                        |
| Source coupling error on the reference side | 0.182                         | - 8.5%                        | 0.192                         | - 2.5%                        |
| Detector coupling error on the target side | 0.222                         | + 11.6%                       | 0.177                         | - 10.2%                       |
| Detector coupling error on the reference side | 0.194                         | - 2.5%                        | 0.192                         | - 2.5%                        |

3.1.2. Correction of optode coupling errors

Figure 6 shows simulated absorption maps, before and after applying the outlier removal algorithm, for high contrast targets with different target radii (0.5, 1.0, and 1.5 cm). It is observed that the optode coupling mismatch has less influence on larger targets. In all cases, the outlier algorithm has successfully identified and removed the measurements from source #9, which had an air gap. Removing these measurements restored the reconstructed image to be almost comparable to the images without mismatch.

Figure 7 shows SSIM values from simulations, before and after applying the outlier removal algorithm, for high contrast targets with different target radii (0.5, 1.0, and 1.5 cm) and depths (1.5, 2.0, and 2.5 cm) from simulations under different coupling mismatch conditions. When the target side has optode coupling errors, the reconstructed images have lower SSIMs than when the optode coupling errors are on the reference side. When there is optode coupling mismatch, for high contrast targets at a fixed depth, smaller targets in general have lower SSIMs than larger targets. For targets of a given size and contrast, usually the deeper the target, the lower the SSIM value under optode coupling mismatch. The proposed outlier removal algorithm increases the SSIMs for most of the tested target depths and sizes, except for cases with coupling errors on the reference side for middle and large size targets at 1.5 cm depth, and the large target at 2 cm depth (marked with red dashed rectangles in Fig. 7(b)). For these three cases, the SSIMs are high (> 0.98) before outlier removal and remain roughly unchanged (percentage change < 0.3) after applying outlier removal.
Fig. 5. Representative absorption maps without and with optode coupling mismatch. (a) No optode coupling error. (b) Optode coupling errors on the source side. (c) Optode coupling errors on the detector side. For the target, $\mu_a = 0.23 \text{ cm}^{-1}$, radius = 1.2 cm, and depth = 2 cm. Of the seven layers in the depth direction, only the first layer containing the target is shown for the simulation and phantom experiments. Each image slice measures 8 cm by 8 cm (from 4 to −4 on the axes) and remains the same for subsequent reconstructed absorption maps. Image artifacts are marked with black ellipses. Color bars indicate the magnitude of the absorption coefficient, in units of cm$^{-1}$. 
Fig. 6. Simulated absorption maps with optode coupling mismatch, before and after outlier removal. The high contrast targets are 2 cm deep. The coupling error was created by shifting the reference side tissue 1.25 cm in the -y direction. Image artifacts are marked with black ellipses.

Fig. 7. SSIMs between no coupling error simulations and with coupling error simulations before and after applying the outlier removal algorithm for high contrast targets with small (0.5 cm), medium (1 cm), and large (1.5 cm) radii. The coupling error was created by shifting the tissue 1.25 cm in the -y direction. Red dashed rectangles marked the cases where outlier removal does not increase SSIMs.
To better demonstrate the performance of the outlier removal algorithm, Fig. 8 shows box plots of SSIMs from simulations under different coupling mismatch conditions. Each group contains 9 high and 9 low contrast targets. The target radii range from 0.5 to 1.5 cm, with a 0.5 cm step size, and the target depths range from 1.5 cm to 2.5 cm, with a 0.5 cm step size. Overall, SSIMs are lower when the coupling errors are on the target side than when the errors are on the reference side (median = 0.965 vs. 0.978 when the source side has coupling errors, and 0.886 vs. 0.986 when the detector side has coupling errors). The outlier removal algorithm successfully corrected most of the image artifacts caused by optode coupling mismatch (p < 0.001), except when the coupling errors occurred on the detector side of the probe when acquiring data from the breast on the reference side, since optode coupling errors do not significantly alter the reconstructed images in this case (SSIM median = 0.986).

![Image](image.png)

**Fig. 8.** Box plot of SSIMs from simulations of high and low contrast targets with different radii and depths under optode coupling mismatch, before and after outlier removal.

Figure 9 shows representative absorption maps for hemispherical phantoms with eight force sensors that indicate real-time optode coupling conditions. In this experiment, the target side was in good contact, as indicated by the force sensors. Compared to the good contact case (Fig. 9(a)), poor contact between the probe and the tissue led to edge artifacts (Fig. 9(b)-(c)), similar to those in Fig. 5, created when the force levels measured by the force sensors near the bad optodes were below the threshold but not necessarily zero. These findings indicate that the force sensor array can capture optode coupling problems and has the potential to monitor coupling conditions in patient studies. The outlier removal algorithm has successfully removed the image artifacts in Fig. 9(b), but the edge artifact is still present in Fig. 9(c) since the algorithm only partially identified all the optodes with bad contact. On the other hand, the force sensors show success in guiding the correction of optode coupling errors in both cases.

### 3.2. Clinical examples

Figure 10 shows tHb maps with optode coupling mismatch errors from patients with a malignant tumor (a) and a benign lesion (b). In Fig. 10(a), from the coregistered US image of a 38-year-old patient with a large stage 2 breast cancer, the 1-cm deep lesion measures 3 cm and 1.3 cm in the x- and z-direction, respectively. The tHb level is high and the distribution is heterogeneous around the tumor periphery, a pattern often seen in large tumors. The proposed outlier removal algorithm successfully identified one edge source with a bad contact. After removing 14 measurements corresponding to this source, the hot spot on the edge close to the source with coupling errors is removed. The maximum reconstructed tHb remains approximately the same, but its distribution is more centered in the tumor region. In (b), a 32-year-old patient with a benign fibroadenoma, the lesion has a depth of 1 cm, and it measures 1.5 cm and 1 cm in the x- and z-directions, respectively. This patient was imaged using a different US-DOT system with 9 sources and 10 detectors [40].
Fig. 9. Original and corrected absorption maps from hemispherical phantom experiments, with eight force sensors indicating real-time optode coupling conditions. A blue force sensor indicates the force level is above the threshold, and an orange sensor indicates below the threshold. The target parameters were $\mu_a = 0.23\ \text{cm}^{-1}$, radius = 1.2 cm, and depth = 2 cm. Corrections using both the outlier removal algorithm and guided by the force sensor status are present. Image artifacts are marked with black ellipses.

The reconstructed hemoglobin has two hot spots close to the edges. After the algorithm processed the data, two sources and one detector at the edges of the probe have bad coupling, and they contribute to a total of 27 measurements. The outlier removal algorithm successfully removes these bad coupling source-detector pairs, and the resulting tHb map correctly shows the lesion in the corresponding region shown in the co-registered US. This example demonstrates that the effect of optode coupling errors on the DOT image is the same for different DOT probes and that the outlier removal algorithm is effective for different probe configurations.
4. Discussion and summary

We used Monte Carlo simulations and phantom experiments to systematically investigate the influence of optode coupling mismatch errors in US-guided DOT. Our results showed that probe-tissue coupling mismatch can produce artifacts in the reconstructed images, appearing as hot spots on the edge or distorted target shapes. Compared to the semi-infinite boundary conditions that we adopted in the forward model, when an optode has a coupling error, it creates an air gap that takes the place of part of the tissue. Because the air does not absorb or scatter photons, photons passing through the air gap will be less attenuated and have a shorter path length, resulting in an increased amplitude and decreased phase in the measured diffuse reflectance. The air gap has other effects on the measured diffused light, such as reducing the light intensity due to reflection at tissue-air and fiber-air interfaces and changing photon propagation directions due to refraction at these interfaces. These findings can provide guidance for system design, operation, and artifact removal in DOT breast imaging, improving the accuracy of diagnosis.
Our studies on optode coupling mismatch errors have several limitations. First, the simulations assumed a pencil beam and detectors receiving photons from all directions. The numerical apertures of the optical fibers, as well as reflection at the tissue-fiber or air-fiber interfaces, were not considered. Second, our simulations and phantom experiments used a hemispherical shape to mimic the breast tissue and did not take into account the variety of breast shapes and densities seen in clinical studies. Third, besides fiber-tissue coupling errors, changes in positioning the probe during data acquisition may also induce other effects, such as changes in the chest wall depth and angle, the tissue heterogeneity, and the vascular volume. These effects were not considered here and need to be investigated in future studies.

To correct optode coupling mismatch errors, we proposed a projection error-based algorithm and demonstrated that it could reduce probe-tissue coupling mismatch errors by removing those measurements corresponding to bad sources/detectors. Its performance in image artifact reduction was demonstrated using simulations, phantom experiments, and clinical data. However, this method may cause a loss of information by reducing the number of measurements from heterogeneous breast lesions. In this study, we apply the outlier removal algorithm only when the objective function is larger than a threshold. This procedure can avoid unnecessarily removing measurements when the modeling errors for all measurements are small. Also, when multiple optodes have coupling errors, this algorithm may fail to fully identify and exactly remove the bad optodes. Lowering the threshold to identify the outliers in measurements (i.e., parameter C in Algorithm 1, step 3) may help to identify more bad optodes, but it may also remove optodes without coupling errors. Elsewhere in the literature, the coupling coefficients are optimized simultaneously with the image reconstruction [25–28]. However, this method adds another set of unknowns and can aggravate the ill-posed nature of the inverse problem. Therefore, a more robust mismatch error correction algorithm needs to be investigated.

Additionally, we designed a resistance-type thin-film force sensor array and demonstrated its ability to minimize optode coupling errors by cueing the operator to make good contact during clinical data acquisition, as well as guiding the coupling error correction in the data processing. However, this prototype is limited because the force sensors are only near the optodes at the boundary of the probe and cannot indicate the precise contact condition of each optode. Thus, ring-shaped sensors around each source and detector could provide better optode coupling feedback in a future design.

In summary, we systemically investigated optode coupling errors that can produce image artifacts and proposed two correction approaches: an outlier removal algorithm that removes the measurements from optode(s) with large model errors, and a force sensor array that can monitor tissue-probe coupling in real-time and guide an operator in achieving good probe contact in data acquisition. Monte Carlo simulations, phantom experiments, and patient examples demonstrated that the outlier removal algorithm and the force sensor array can reduce the optode coupling errors and improve DOT imaging quality. Our approaches and study results have significant implications for reducing image artifacts from the fiber-optic-based handheld probes popular in DOT and DOS devices.

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