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10	
11	Noise estimation in infrared image sequences: a tool for the
12	quantitative evaluation of the effectiveness of registration
13	algorithms
14	
15	
16	Abstract — Dynamic infrared imaging has been proposed in literature as an adjunctive technique to
17	mammography in breast cancer diagnosis. It is based on the acquisition of hundreds of consecutive
18	thermal images with a frame rate ranging from 50 frames/s to 200 frames/s, followed by the harmonic
19	analysis of temperature time series at each image pixel. However, the temperature fluctuation due to
20	blood perfusion, which is the signal of interest, is small compared to the signal fluctuation due to subject
21	movements. Hence, before extracting the time series describing temperature fluctuations, it is
22	fundamental to realign the thermal images to attenuate motion artifacts. In this paper, we describe a
23	method for the quantitative evaluation of any kind of feature-based registration algorithm on thermal
24	image sequences, provided that an estimation of local velocities of reference points on the skin is
25	available. As an example of evaluation of a registration algorithm, we report the evaluation of the signal
26	to noise ratio improvement obtained by applying a non-rigid piecewise linear algorithm.

27

Index Terms—Dynamic infrared imaging, image registration, signal-to-noise ratio estimation, thermal
 image sequence, breast cancer detection.

30

I. INTRODUCTION

31 Currently, the screening gold standard in breast cancer diagnosis is mammography. Since the early seventies, thermography has been proposed as a possible adjunct to mammography in screening, but static 32 33 thermography - i.e., the simple measurement of breast skin temperature - yielded no satisfactory results [1]. More recently, Dynamic Area Telethermometry (DAT) [2-3], also known as Dynamic InfraRed 34 35 Imaging (DIRI) [4-5], has been proposed as a new imaging modality for breast cancer detection. It 36 requires the acquisition of a sequence of hundreds of consecutive thermal images with a rate ranging from 50 frames/s to 200 frames/s. The harmonic analysis of the time course of temperature fluctuations allows 37 to obtain information on the local blood perfusion. In literature, it has been reported that temperature 38 fluctuations have an important diagnostic value in oncology [2-3]. In fact, recent studies have 39 40 demonstrated that cancer-associated extra vascular nitric oxide determines a perturbation in the normal 41 modulation of the local blood flow, which can be detected through the analysis of the fluctuations of temperature at each sample region [2-5]. Hence, after subdividing the region of interest in square sub-42 regions (approximately 4 mm² each) consisting of one or more pixels, spectral analysis of the temperature 43 time series corresponding to each sub-region is performed. 44

In our experimental protocol, the acquisition of the image sequence lasts 10 seconds, during which the patient's breast moves non-rigidly due to physiological (breathing, heart activity, ...) and random movements. Consequently, the signal of interest, i.e., the small temperature fluctuations due to perturbations of the blood perfusion in a certain region, is superimposed to signal fluctuations arising from the subject motion. This is because temperature samples corresponding to different skin regions are recorded as belonging to the same region observed by the infrared sensor. Motion artifacts are then particularly relevant in areas in which a strong spatial gradient of temperature is present. Therefore, before proceeding with the harmonic analysis of the temperature time series in each square sub-region, it is fundamental to properly realign the thermal images composing the sequence to attenuate motion artifacts. Although some Authors have reported the detrimental effect of motion artifacts [4], at this time there is no quantitative evaluation of the power due to the effects of motion artifacts with respect to that of the signal of interest. This also limits the possibility of objectively evaluating the performance of different algorithms for realigning infrared sequences [6].

The goal of this paper is to propose a method to quantitatively evaluate the performances of markerbased registration algorithms in dynamic infrared imaging, in terms of improvement of the signal to noise ratio. This approach can be applied to any kind of registration algorithm based on control points, provided that an estimation of local image velocities is available. We then present the results obtained by applying the proposed approach to evaluate the improvement of the signal to noise ratio obtained through a piecewise linear registration algorithm applied to sequences relative to three subjects with different breast size.

65

II. MATERIALS AND METHODS

66 A. The model

First, we introduce a model for the noise estimation in dynamic infrared imaging. Considering a small portion of skin and indicating by T(x,y,t) the temperature that the infrared sensor measures in the point (x,y) at a given time instant *t*, temperature variations in time captured by the infrared camera are a combination of the physiological variations of the skin temperature (the signal of interest) and of apparent temperature changes actually due to patient's movements (noise).

72 The total derivative of temperature with respect to time, dT/dt, is:

73

74

$$\frac{dT}{dt} = \frac{\partial T}{\partial t} + \frac{\partial T}{\partial x} \frac{\partial x}{\partial t} + \frac{\partial T}{\partial y} \frac{\partial y}{\partial t} =$$

$$= \frac{\partial T}{\partial t} + (\vec{v} \cdot \nabla)T$$
(1)

where $\frac{1}{V}(v_x, v_y)$ is the 2-dimensional velocity of the skin portion and ∇T is the spatial temperature gradient. Equation 2 reports the expression of the noise N(x, y, t) introduced by motion artifacts.

77
$$N(x, y, t) \approx \int_{0}^{t} \vec{v}(x, y, t') \cdot \nabla T(x, y, t') dt'$$
(2)

A measure of the performance of a realignment algorithm applied to the infrared image sequence is the improvement of the signal-to-noise ratio obtained through the registration. The signal-to-noise ratio of the process - at each point (x,y) - is defined as $S/N \equiv \sigma_T^2(x,y)/\sigma_N^2(x,y)-1$, where $\sigma_T^2(x,y)$ is the variance of the measured temperature time series T(x,y,t) (signal plus noise) and $\sigma_N^2(x,y)$ is the variance of the noise, as given by Eq. (2). Similarly, we define the signal-to-noise ratio after registration as $(S/N)_R \equiv \sigma_{T_R}^2(x,y)/\sigma_{N_R}^2(x,y)-1$, where $\sigma_{T_R}^2(x,y)$ is the variance of the measured temperature time series $T_R(x,y,t)$ obtained after sequence realignment and $\sigma_{N_R}^2(x,y)$ is the variance of the series $T_R(x,y,t)$ obtained after sequence realignment and $\sigma_{N_R}^2(x,y)$ is the variance of the series to the variance of the variance of the variance of the variance of the series $T_R(x,y,t)$ obtained after sequence realignment and $\sigma_{N_R}^2(x,y)$ is the variance of the series to the variance of the variance of the variance of the variance of the series $T_R(x,y,t)$ obtained after sequence realignment and $\sigma_{N_R}^2(x,y)$ is the variance of the series to the variance of the variance of the variance of the variance of the series $T_R(x,y,t)$ obtained after sequence realignment and $\sigma_{N_R}^2(x,y)$ is the variance of the series $T_R(x,y,t)$ obtained after sequence realignment and $\sigma_{N_R}^2(x,y)$ is the variance of the series $T_R(x,y,t)$ obtained after sequence realignment and $\sigma_{N_R}^2(x,y)$ is the variance of the section $T_R(x,y,t)$ obtained after sequence realignment and $\sigma_{N_R}^2(x,y)$ is the variance of the section $T_R(x,y,t)$ obtained section $T_R(x,y,t)$ is the variance of the section $T_R(x,y,t)$ is the variance in $T_R(x,y,t)$ is the vari

85 term $\int_{0}^{t} \vec{v}_{R}(x, y, t') \cdot \nabla T_{R}(x, y, t') dt'$, being $\vec{v}_{R}(x, y, t)$ the residual velocity, not compensated by the

86 registration algorithm.

87 B. Acquisition system and patient positioning

The infrared image sequences were acquired with an AIM256Q camera (Long Wave Quantum Well Infrared Photodetector, 256×256 pixels, produced by AEG Infrarot-Module GmbH, Germany). The acquisition time was equal to 10 seconds and the frame rate was 50 frames/s; hence, each sequence consisted of 500 thermal images of 256×256 pixels.

The sensor noise declared by the constructor of the infrared camera is equal to 17.3 mK (given as NETD, with an integration time of 20 ms) and thus is negligible compared to noise due to patient's movement, estimated by simulations, which is typically of the order of hundreds of mK. Hence, in our model, we considered the patient's movement as the only noise source.

96 The patient was asked to lie down onto an examination table with a backrest inclination of 40 degrees

with respect to the horizontal plane. She was also asked to raise up her arms with the hands resting overher head. We acquired a frontal view comprehending both breasts.

Before the acquisition, two sets of wooden spherical markers (5 mm in diameter) were applied to the skin to obtain a) control points, i.e. contrasted features for registration, and b) test points, for evaluating the goodness of the registration itself. In particular, as control points we placed 6-8 equally spaced markers around each breast contour, one roughly at the center of the previous ones, and 2 on the sternum. Test points consisted of markers applied internally to each breast contour. All markers were fixed to the skin by means of biocompatible glue. Figure 1a shows a typical placement of control points (light-colored markers) and of test points (dark markers).

106

III. IMAGE REGISTRATION AND REGISTRATION EVALUATION

107 A. Image Registration

The first step in any feature-based registration is the detection of the control points that are used to compute the transformation. To localize control and test points, we developed a specific algorithm for the automatic segmentation of the image and labeling of markers [6].

111 Centroids of control points were used to obtain a piece-wise linear transformation based on a Delaunay 112 triangulation [7] of the region to be registered. Figure 1b shows an example of triangulation. We chose 113 this specific transformation because it is reported to give good results when small geometric differences 114 between the images to be registered are expected [8], as in this case.

Here we reported the specific registration algorithm we adopted only for the sake of completeness, but we emphasize that the signal-to-noise ratio estimation method we propose can be applied to any kind of registration algorithm based on control points, if an estimation of local image velocities is available.

118 B. Registration Evaluation

In order to evaluate the signal-to-noise ratio before and after the registration, we estimated the velocities \vec{v} and \vec{v}_R . We tested, on the three subjects that were included in this paper, different algorithms to 121 interpolate the velocities, both in the registered and in the non-registered sequences. We benchmarked the 122 results using Nearest-Neighbors (NN), Linear Interpolation (LI), and Biharmonic Spline Interpolation (SI), for estimating the velocities within the region of interest. Results, in terms of SNR quantification, 123 were different from subject to subject: for subject 1 (small breast size) LI was better than the others, for 124 125 subject 3 (large breast size) NN was the best, and for subject 2 (medium breast size) all the techniques behaved similarly. Specifically, considering the three interpolation techniques applied to subject 2 126 127 (medium breast size) in terms of SNR increment due to registration no statistical significance was found (Student's t-test, P > 0.05). Presently, our results do not show any significant difference among the 128 techniques we tested. We chose NN since we believe it gives acceptable results in most of the tested 129 conditions and for the majority of the subjects (medium breast size). To this purpose, we calculated the 130 Voronoi regions [9] associated to test marker centroids (see Fig. 1c) and assumed that the points 131 132 belonging to the same Voronoi region had equal velocity.

The instantaneous velocity \vec{v} of a certain marker centroid ($\mathbf{x}_t, \mathbf{y}_t$) at time *t* was calculated using a twopoint forward approximation:

135
$$\mathbf{v}_{\mathbf{x},t} = \frac{\mathbf{X}_{t+1} - \mathbf{X}_{t}}{\Delta t}; \mathbf{v}_{\mathbf{y},t} = \frac{\mathbf{y}_{t+1} - \mathbf{y}_{t}}{\Delta t},$$

136 where $\Delta t = 20$ ms is the sampling period.

The image gradient is computed using the digital approximation of the first order derivative in its antisymmetrical and linear implementation, i.e. by convolving the image with the vector [-0.5 0 0.5]).

139

IV. UNCERTAINTY IN SNR CALCULATION

The SNR depends on velocities and temperature gradients as stated by Eq. 2. In this Section we show how the localization error affects the SNR estimation and we provide a worst-case estimate of the uncertainty.

143 The uncertainty on the SNR may be expressed by the uncertainty on the noise computed according to 144 Eq. 2, in which \vec{v} and ∇T are independent variables. Let u(x) end u(y) be respectively the uncertainty on the localization of marker centroids along *x* and *y*. The uncertainty on the noise value is expressed byEq. 3.

147
$$u(N(x, y, t)) = \sqrt{\left(\frac{\partial \int_{0}^{t} \vec{v}(x, y, t') \cdot \nabla T(x, y, t') dt'}{\partial x}u(x)\right)^{2} + \left(\frac{\partial \int_{0}^{t} \vec{v}(x, y, t') \cdot \nabla T(x, y, t') dt'}{\partial y}u(y)\right)^{2}} \quad (3)$$

By applying the partial derivative operator on the first term of Eq. 3 we obtain Eq. 4, in which, by assuming the tissue as locally inextensible ($\frac{\partial \vec{v}(x, y, t')}{\partial x} = 0$), we can neglect the first term.

150
$$\frac{\partial \int_{0}^{t} \vec{v}(x, y, t') \cdot \nabla T(x, y, t') dt'}{\partial x} = \int_{0}^{t} \left[\frac{\partial \vec{v}(x, y, t')}{\partial x} \cdot \nabla T(x, y, t') + \vec{v}(x, y, t') \cdot \frac{\partial \nabla T(x, y, t')}{\partial x} \right] dt'$$
(4)

t

The second term of Eq. 3 may be treated similarly. Assuming that the behavior along *x* and *y* is similar,
the two terms of Eq. 3 may be considered as equal. It follows that

153
$$u(N(x, y, t)) = \sqrt{2 \cdot \left[\int_{0}^{t} \vec{v} \cdot \frac{\partial \nabla T}{\partial x} dt'\right]^{2} \cdot \left[u(x)\right]^{2}} \cong \sqrt{2 \cdot \left[\frac{\Delta x}{\Delta t} \cdot \frac{\partial \nabla T}{\partial x} \cdot \Delta t\right]^{2} \cdot \left[u(x)\right]^{2}}$$
(5)

154 Posing $\Delta x = 0.1 \,\mathrm{px}$, $\frac{\partial \nabla T}{\partial x} = 0.25 \,\mathrm{K} \cdot \mathrm{px}^{-2}$, $u(x) = 0.015 \,\mathrm{px}$ (values obtained from our database of images

using a 8-time oversampling [6]), we obtain a value of noise uncertainty of the order of 0.5 mK. After realignment with a piecewise linear algorithm we have a residual error approximately equal to 20 mK, and hence forty times larger than noise uncertainty. Hence, the uncertainty on the SNR value is approximately 0.25 dB.

In order to test the dependence of the proposed SNR measure on the accuracy of the calculated velocities we performed a robustness analysis considering different registration transformations: PieceWise Linear (PWL), Polynomial of order 4 (P4), and Linear Conformal (LC), i.e., a transformation that can include a rigid roto-translation, and/or a scaling. The uncertainty on the localization of marker centroids ranges from 0.015 to 0.022 px for the three registration transformations. The corresponding uncertainty on the measure of the SNR is less than 0.4 dB in the worst case.

165

V. RESULTS

The three subjects whose results are reported in this paper had respectively small breast size (cup A, 166 subject 1), medium breast size (cup B, subject 2), and large breast size (cup DD, subject 3). 167 Fig. 1a shows the two sets of markers applied to subject 3 (large breast size), whereas Fig. 1b depicts a 168 thermographic shot of the same subject showing superimposed (black lines) the Delaunay triangulation 169 170 used in the registration procedure. Figure 2 summarizes the results relative to these subjects. For each subject we report some parameters 171 172 describing the signal-to-noise ratio relative to the Region Of Interest (ROI) before and after applying the registration algorithm. Specifically, we report the values of the median, 25th and 75th percentiles, 173 minimum and maximum of the signal-to-noise ratios expressed in decibels. The ROI is defined as the area 174 175 contained within the perimeter constituted by the outer triangulation lines. Notice that this ROI is slightly changing over time. However, given the small percentage of pixels entering/exiting the ROI with respect 176 to the minimum-area ROI (less than 2 %), we decided to discard these pixels and to consider the same 177 ROI for all the frames of the sequence. 178

Considering the three subjects above described, before registration, the signal-to-noise ratio median ranged from 1 to 2 dB (thin line boxes), whereas, after registration, it increased up to 9 dB, thus demonstrating that registration causes a decrement of the noise power due to motion artifact as high as 5-6 times, depending on the subject.

183

VI. CONCLUSION

In this paper, we present a methodology to estimate the noise due to patient motion that affects an infrared image sequence. In turns, the knowledge of noise power allows to estimate the signal-to-noise ratio that characterizes the sequence.

187 Results herein presented demonstrate that, as long as the assumptions on which the noise model is

based hold, it is possible to compute the signal-to-noise ratio of a specific infrared sequence of images.
This is an original and important result, since it allows to assess objectively the effectiveness of different
registration algorithms, as well as to obtain a quantitative evaluation of the quality of an infrared sequence
of images.

The evaluation of the ROC curves of any detector used to differentiate sequences obtained from normal or pathological subjects is not possible without the knowledge of the signal-to-noise ratio of the sequence. Hence, we believe this noise estimation method will crucial to fill a gap that currently limits the possibility of further improving the results given by dynamic infrared imaging in early breast cancer detection and, consequently, also limits its spreading in clinics.

197

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225

226

227 Figures captions

- Fig. 1a. Picture of subject 3. Control points are represented by light-colored markers, while test points by
- dark markers. Fig. 1b-c. Single frame extracted from the infrared sequence: Delaunay triangulation is
- shown superimposed (Fig. 1b); Voronoi regions are shown superimposed (Fig. 1c).

231

232

Fig. 2. Boxplot of the signal to noise ratio (SNR) before (thin line) and after (thick line) registration for

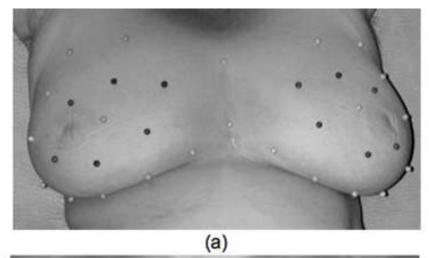
three different subjects respectively with small (subject 1), medium (subject 2) and large (subject 3) breast

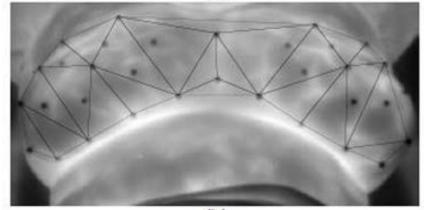
- size. Each box reports the median value, percentiles (25th and 75th), minimum and maximum representing
- 236 the SNR(x,y) distribution relative to the region of interest.

237

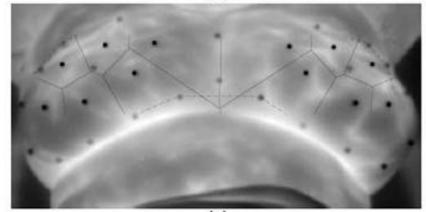
Figura 1 238

239





(b)



(C)

