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Fusion of 3D real-time echocardiography and cine MRI using a saliency analysis

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1 **Fusion of 3D real-time echocardiography and cine**
2 **MRI using a saliency analysis**

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6
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8 **Abstract**

9 **Purpose:**

10 This paper presents a novel 3D multimodal registration strategy to fuse 3D
11 real-time echocardiography images with cardiac cine MRI images. This align-
12 ment is performed in a saliency space, designed to maximize similarity between
13 the two imaging modalities. This fusion improves the quality of the available
14 information.

15 **Methods:**

16 The method performs in two steps: temporal and spatial registrations. A tem-
17 poral alignment is firstly achieved by non-linearly matching pairs of correspon-
18 dences between the two modalities using a dynamic time warping. A temporal
19 registration is then carried out by applying non-rigid transformations in a
20 common saliency space where normalized cross correlation between temporal
21 pairs of salient volumes is maximized.

22 **Results:**

23 The alignment performance was evaluated with a set of 18 subjects, 3 with
24 cardiomyopathies and 15 healthy, by computing the Dice score and Haus-
25 dorff distance with respect to manual delineations of the left ventricle cavity
26 in both modalities. A Dice score and Hausdorff distance of 0.86 ± 0.04 and
27 13.61 ± 3.86 mm respectively were obtained. In addition, the deformation field

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was estimated by quantifying its foldings, obtaining a 98% of regularity in the deformation field.

Conclusions:

The 3D multimodal registration strategy presented is performed in a saliency space. Unlike state of the art methods, the presented one takes advantage of the temporal information of the heart to construct this common space, ending up with two well aligned modalities and regular deformation fields. This preliminary study was evaluated on heterogeneous data composed by two different datasets, healthy and pathological cases, showing similar performances in both cases. Future work will focus on testing the presented strategy in a larger dataset with a balanced number of classes.

Keywords Image registration · spatio-temporal saliency · cardiac cine MRI images · echocardiography

1 Introduction

Cardiac imaging plays an important role in diagnosis and treatment planning of prevalent heart diseases. Non-invasive procedures, specifically 3D real-time echocardiography (3DUS+t) and cine cardiac MRI (cMRI), provide structural and functional information of the heart. While 3DUS+t is a first option for cardiac evaluation and follow-up, cMRI is used when a diagnosis doubt persists after the ultrasound examination [9]. In pathologies such as pulmonary arterial hypertension, ischaemic heart disease, arrhythmogenic ventricular cardiomyopathy and atrial arrhythmias [24,18,2], the information obtained with these two modalities results to be complementary. Under these considerations, multimodal image fusion should provide a more accurate and reliable examination by combining morphological (cMRI) and functional (3DUS+t) assessments [18,24]. This fusion could facilitate anatomo-functional correlations of cardiac abnormalities that lead to design new diagnostic and follow-up markers [6,17,2] to detect early impairments and subtle changes in the cardiac function. Consequently, a better therapy follow-up could be performed to improve patient categorization, personalized treatment and survival.

Image fusion is generally carried out by a registration process [12]. However, a useful registration between 3DUS+t and MRI images is a complex and difficult process, basically because the represented information is captured using very different physical sensors. Furthermore, 3DUS+t images have a lower signal-to-noise ratio (SNR) than 2DUS+t images. There are also several factors that increase a poor definition of the left ventricular chamber and walls during the acquisition in echocardiography, such as anatomic particularities (obesity, asthenic habitus) and other related information, such as acquired disease that affects the acoustic window.

Few works in the state of the art have addressed the challenge of registering 3D echocardiography and cine MRI images. These approaches can be divided in two groups: intensity-based registration [10,28,13] and surfaced-based registration [15,20]. In the first group, works map MRI and 3DUS modalities to a

71 common space using only spatial information. Some of them transformed both
 72 modalities into their corresponding phase maps using Fourier transform [28].
 73 However, in some cases, this phase representation is very similar to the orig-
 74 inal image and may lead to erroneous registrations. Other works [10,13,27]
 75 align the modalities in the intensity space, where the registration is prone to
 76 error due to the high data heterogeneity and the noisy US images. For the
 77 second group, surfaced-based registration, cardiac structures are segmented
 78 in both modalities and then, a surface extracted from one modality is non
 79 rigidly-registered to the other surface modality. In this group, strategies based
 80 on the registration of common landmarks in both modalities are also taken
 81 into account. Nevertheless, these approaches are highly sensitive to the seg-
 82 mentation and precise setting of landmarks, due to the inter- and intra-shape
 83 variability of the heart, its complex dynamic and the image quality.

84 Unlike these works, which are based only on spatial registration or surface
 85 deformations, this paper proposes a novel 3D multimodal registration frame-
 86 work by combining saliency and temporal information, which is applied to
 87 cMRI and 3DUS+t images. In this work, a non rigid deformation is performed
 88 to cope with local differences between images, since that heart is intrinsically
 89 deformable, even if intra-patient cases are considered. Although a preliminary
 90 work of this study has been previously published as a conference paper [30],
 91 this paper is substantially different from that work in that it incorporates an
 92 initial registration to perform a more robust alignment between both modal-
 93 ities and it includes more experimental validation results and the use of quan-
 94 titative metrics for the evaluation.

95 The paper is organized as follows: In Section 2 the registration framework
 96 is described. Experiments and results are provided in Section 3. Finally, con-
 97 clusions are presented in Section 4.

98 2 Methodology

99 Each image modality (cMRI noted as MR and 3DUS+t noted as US) is rep-
 100 resented as a sequence $I(x, y, z, t)$ of images, where $(x, y, z) \in \Omega_I$ corresponds
 101 to the spatial coordinates in the domain of the image (Ω_I) and $t \in \{1, T\}$
 102 represents a temporal position in the sequence, being T the number of frames
 103 per cardiac cycle for each modality, MR and US, which can be different, i.e.,
 104 T^{mr} and T^{us} . This work proposes a 3D registration strategy to map each voxel
 105 of the moving modality to its corresponding voxel in the reference modality.
 106 The registration process is decoupled into two temporal and spatial steps of
 107 alignment, that are hereafter described.

108 2.1 Temporal alignment

109 Firstly, a temporal alignment sets the frame correspondences between both
 110 image sequences. For doing so, two sub-steps are performed: i) an image-

111 based cardiac dynamic descriptor and ii) a nonlinear mapping between both
 112 modalities, using the method proposed by Betancur et al [4].

113 2.1.1 Image-based cardiac dynamic descriptor.

114 A $\Phi(t; I)$ curve that describes events of the cardiac cycle consistently [19,
 115 27,4] is constructed using all volumes or image sequence I_t of the cardiac
 116 cycle. This process is independently performed for each image sequence I_t , by
 117 computing the similarity between the volume at the end of the diastole (ED)
 118 with respect to each of the remaining volumes of the cycle, Eq. 1. The ED
 119 frame is arbitrarily set to the first frame of the sequence, $I_{t=1}$. The classical
 120 normalized cross correlation is used as similarity measure since this measure
 121 is less sensitive to different noisy conditions.

$$122 \quad \Phi(t; I_t) = \left\langle \frac{I_{t=1} - \bar{I}_{t=1}}{\|I_{t=1} - \bar{I}_{t=1}\|}, \frac{I_t - \bar{I}_t}{\|I_t - \bar{I}_t\|} \right\rangle \quad \forall t \in \{1, T\} \quad (1)$$

123 being \bar{I}_t the average intensity value of the image I_t .

124 2.1.2 Nonlinear mapping between the images in the reduced space.

125 Due to the non-linear nature of the cardiac function, a dynamic time warping
 126 (DTW) [3] is applied to map each point of the curve $\Phi^{mr}(t)$ to its correspond-
 127 ing point of the curve $\Phi^{us}(t)$, being $\Phi(t)$ the curve described in equation 1. As
 128 a result of this mapping, a set of aligned temporal pairs $A = \{(t_i^{us}, t_j^{mr})\}$ is
 129 obtained for each subject. Despite that several US volumes could be matched
 130 with the same MR volume or the other way around, this does not pose any
 131 issue because this temporal alignment matches volumes that are close in time
 132 and from the same cardiac phase.

133 2.2 Spatial alignment

134 A main contribution of this work is to spatially register the image sequences by
 135 using spatio-temporal information of the cardiac function in the 3D domain.
 136 For doing such registration, two sub-steps are performed: i) mapping the image
 137 sequence to a common saliency space and ii) setting customized registration
 138 metric in the saliency space.

139 2.2.1 Mapping the image sequence to a saliency space.

140 Multimodal cardiac images are statistically dependent by the fact of being cap-
 141 tured from the very same object, i.e., the heart, and such dependency could be
 142 used to fuse them. The human visual system (HVS) is able to extract relevant
 143 information by decomposing the scene into low level representations which are
 144 integrated and encoded as visual information [22]. Under such hypotheses, the

145 salient volume is built upon a multi-scale region-based decomposition which
 146 preserves the most correlated information and is obtained by applying a classic
 147 Gaussian pyramidal filtering [5]. For every image sequence, five scales s are
 148 taken, namely the original scale, a finer level and three incrementally coarser
 149 levels of the original. The finer level provides more details of the heart, while
 150 the coarser levels provide a global localization of the heart. For each scale s ,
 151 regions r are extracted by using the simple linear iterative clustering (SLIC)
 152 algorithm [1]. The Cartesian coordinates of these regions are stored as a grid
 153 G since every processing is from here on performed exclusively within this
 154 grid. Afterwards, each image is filtered for each scale s and for each instant
 155 of the time t by applying steerable filters [7]. These filters correspond to an
 156 oriented first derivative of a 3D Gaussian with a standard deviation set to 3,
 157 due to the noise in cMRI and 3DUS images can be modeled by Gaussian or
 158 Laplacian distribution [29]. The result of this bank of filters is an image SV_t
 159 for each scale s where their structural features, such as intensity, orientation
 160 and edges, are enhanced, while it reduces noise.

161 Saliency is defined by a consistent difference between regional r features
 162 and their surroundings during the time, Eq. 2. Independently of each scale s ,
 163 the salient volume at time t is estimated by comparing it with respect to the
 164 remaining frames. This ensures temporal coherence of the salient region, even
 165 in scenes with a higher level of complexity, such as low frame rate and noisier
 166 sequences [11,26].

$$167 \quad \text{saliency}(t, r, s) = \sum_{\tau \in T} |SV_t(r, s) - SV_\tau(r, s)|^2 \quad \forall r \in G \quad (2)$$

168 The final salient volume S is obtained by averaging saliency for every scale,
 169 previously set to the original size either by interpolation or decimation. This set
 170 of salient volumes constitutes the saliency space. Figures 1 and 2 show exam-
 171 ples of saliency measured in echocardiography and magnetic resonance imaging
 172 respectively. Observe how the myocardium is highlighted in both modalities.
 173 This representation provides a common space where both image modalities
 174 can be spatially aligned.

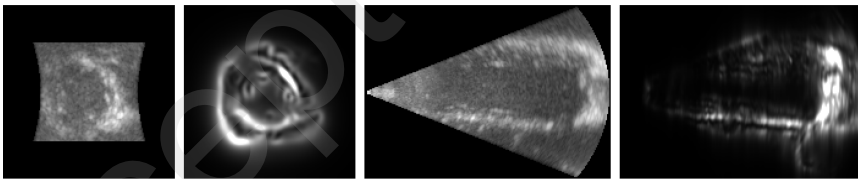


Fig. 1 Salient images in echocardiography. Panels from left to right: original image in axial view, salient image in axial view, original image in coronal view and salient image in coronal view.

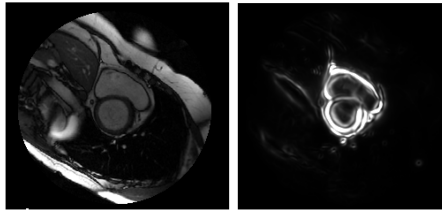


Fig. 2 Saliency image in short axis cine MRI. Left panels shows the original image and the right panel illustrates its respective saliency.

175 2.2.2 Setting customized registration metric in the saliency space.

176 Since the field of view is not the same in both modalities, a coarse manual
 177 delineation of the epicardium of the left ventricle (LV) at the end of the diastole
 178 (ED) is obtained to delimit a common region of interest (ROI). Herein, this LV
 179 ROI is used for the whole cardiac cycle, under the hypothesis that myocardium
 180 contracts towards the center of the LV and such ROI encloses all the cardiac
 181 structures of interest [16].

182 The intensity image sequence I_t , the LV ROI and the saliency image S
 183 are oriented to the same Right-Anterior-Inferior radiological coordinates RAI ,
 184 defining a common x, y, z order, using the ITK-snap tool [25]. This orientation
 185 only describes the mapping from the voxel coordinate system to the phys-
 186 ical coordinate system. As 3DUS+t modality has a higher spatial resolution
 187 than cMRI, the oriented LV ROI, the salient volume and the intensity im-
 188 age sequence from cMRI modality are linearly resampled to obtain the same
 189 dimensions and voxel size of the echocardiographic image. Figure 3 shows a
 190 resampled MRI image for a healthy subject in the longitudinal direction.

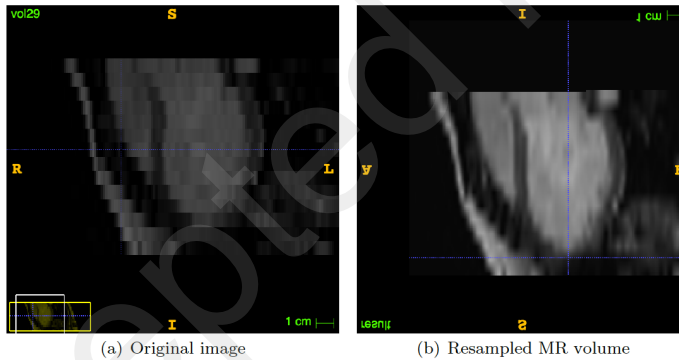


Fig. 3 Example of a resampled MRI volume in the longitudinal direction.

191 Afterwards, a spatial registration is performed in the saliency space de-
 192 limited by the LV ROI. For each temporal pair $(t_i^{us}, t_j^{mr}) \in A$ obtained as
 193 described in section 2.1, a mapping-salient function \mathcal{F}_t sets each voxel in the

194 cMRI image to its corresponding voxel in the 3DUS domain at the instant
 195 of time $\hat{t} = (t_i^{us}, t_j^{mr})$. The mapping-salient function for each temporal pair is
 196 then defined as:

$$197 \quad \mathcal{F}_{\hat{t}}(S_{t_i}^{us}, S_{t_j}^{mr}) = \underset{T_x}{argmax} \quad sim(S_{t_i}^{us}, S_{t_j}^{mr}(T_x); T_x) \quad (3)$$

198 where T_x is a transformation model that maximizes the similarity (*sim*)
 199 between both salient volumes, $S_{t_i}^{us}$ and $S_{t_j}^{mr}$. In this work, T_x is a non-rigid
 200 transformation applied to the salient volumes via interpolation with a B-spline
 201 of order 3 that maximizes the normalized cross correlation. This similarity
 202 measure is used since it is invariant to affine intensity distortions [8]. Herein,
 203 an adaptive stochastic gradient descent [14] was used as optimizer. In order to
 204 achieve an accurate alignment, this non-rigid registration was initialized by an
 205 Eulerian transformation [21] that rigidly aligns the LV ROI centroids of both
 206 modalities.

207 Once the mapping-salient function $\mathcal{F}_{\hat{t}}$ is obtained for each temporal pair
 208 \hat{t} , it is applied to the original image sequence cMRI, $I_{t_j}^{mr}(\mathcal{F}_{\hat{t}})$, mapping it to
 209 the 3D echocardiography image domain $I_{t_i}^{us}$. This process is applied for all
 210 the aligned temporal pairs and in consequence, the whole cMRI sequence is
 211 covered.

212 3 Experiments and results

213 3.1 Image Data

214 Two datasets of pairs of cMRI and 3DUS+t data were used: healthy subjects
 215 and pathological subjects.

216 3.1.1 Healthy group.

217 This group comprises 15 healthy subjects [23]. cMRI and 3DUS+t acquisitions
 218 were obtained within an interval of 3.5 ± 3.3 days. Acquisition features for
 219 cMRI and 3DUS+t are, respectively: temporal resolution of 30 and $14.93 \pm$
 220 3.03 frames per second; slice thickness of 8 mm and 0.71 ± 0.09 mm; and in-
 221 plane resolution voxel size of 1.22 ± 0.05 mm and 0.84 ± 0.16 mm. Delineated
 222 volumes of the left ventricle cavity are provided with each modality for all the
 223 cardiac cycle.

224 3.1.2 Pathological group.

225 It is composed of 3 subjects with dilated and hypertrophic cardiomyopathy,
 226 who followed an acquisition protocol comprising both cMRI and 3DUS+t. This
 227 dataset was acquired at CHU-Pontchaillou in Rennes, France. This study was
 228 part of a systematic database review conducted following the Declaration of
 229 Helsinki and approved under the CNIL (National Commission on Informatics

and Liberty of France). Acquisition features for cine MRI and 3DUS+t were, respectively: temporal resolution of 28.33 ± 5.77 and 22.33 ± 14.98 frames per second; slice thickness of 8 mm and 0.74 ± 0.11 mm; and in-plane resolution voxel size of 1.62 ± 0.1231 mm and 1.08 ± 0.15 mm. Delineated volumes of the left ventricle cavity are manually provided in each modality at the end of the diastole and end of the systole.

The method performance was evaluated for each step, temporal and spatial alignment, as follows.

3.2 Evaluation of the temporal alignment

The temporal alignment was validated for each image modality and dataset by computing the Mean Absolute Error (MAE) between the time point corresponding to the end of the systole (ES), which was manually set by an experienced observer, and the time point with the minimum value of the curve Φ obtained in Section 2.1.1. This MAE measures the distance in number of frames between the ES position estimated by the method and the position set by the expert. The MAE for the healthy group was 2.73 ± 1.67 frames and 0.93 ± 0.70 frames for cMRI and 3DUS+t, respectively. While the MAE for the pathological group was 1.0 ± 1.0 frames and 2.33 ± 1.53 frames for cMRI and 3DUS+t, respectively.

3.3 Evaluation of the spatial alignment

The results differ according to the temporal duration and the phases that were considered in the saliency estimation. Different tests have been conducted, along the heart cycle providing the results presented in the paper and along each cardiac period (diastole and systole) providing some differences. These second results showed a slight difference in accuracy about the 5%. In this sense, the complete cardiac cycle is used to compute the saliency in each modality.

Qualitative results of the spatial alignment are illustrated for one pathological case in Fig. 4, from the base to the apex (in rows) at four instants of time presented in the columns (End of the diastole ED, end of the systole ES, intermediate time between the ED and ES, and intermediate time between the ES and the final frame). Observe the good spatial alignment between cMRI (green color) and 3DUS+t (magenta color) volumes using the saliency descriptor and the registration framework, in particular for the basal, basal-mid and mid views, i.e., the myocardium is good overlapped in both modalities.

To quantitatively evaluate the registration performance, aligned delineations of the LV cavity from both modalities were compared at the ED and ES by computing the Dice Score and Hausdorff distance.

Table 1 and Fig. 5 show the spatial registration performance of the presented strategy, when it is evaluated in terms of the Dice score and Hausdorff

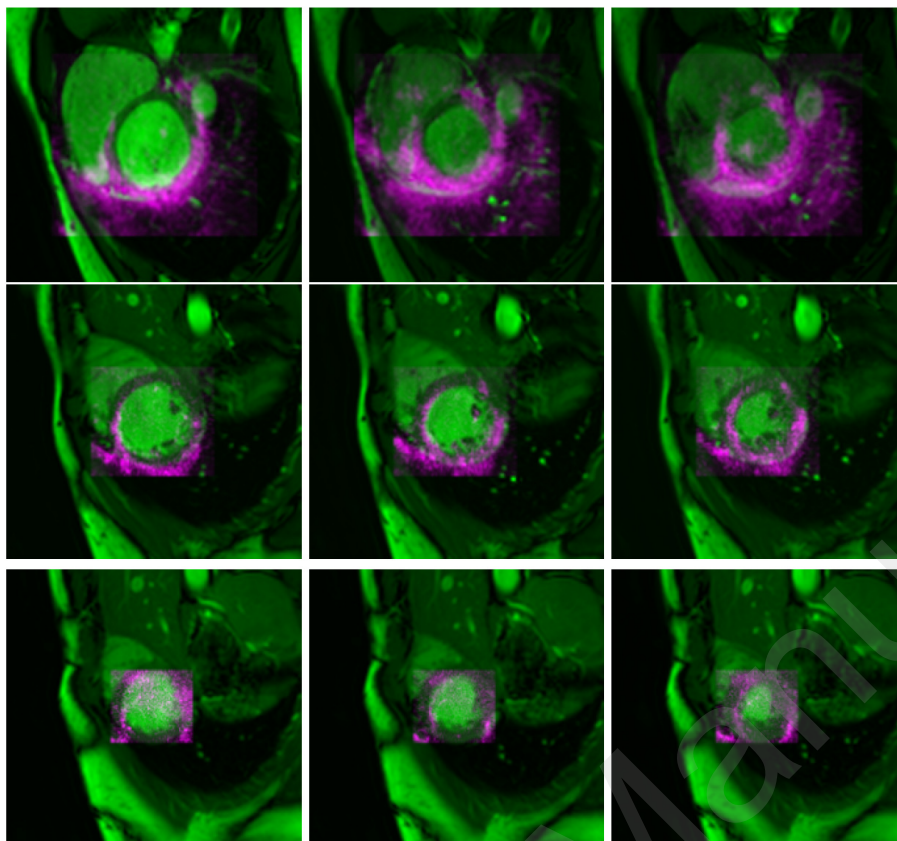


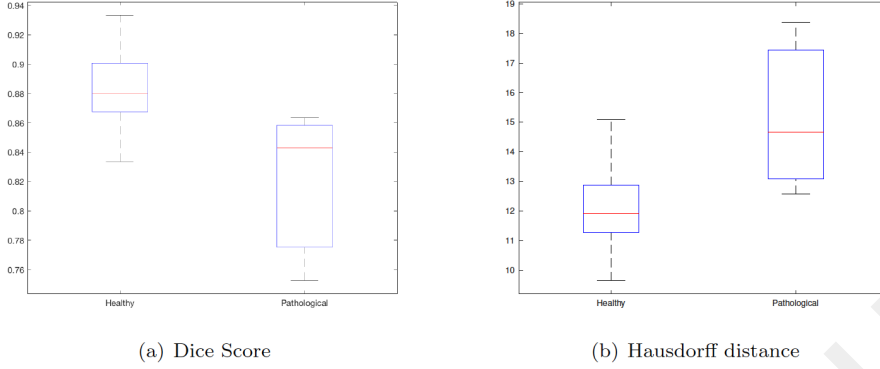
Fig. 4 Illustration of a spatial alignment for one pathological case. MRI (green color) superimposed to the 3DUS (magenta color). Rows correspond to the volume levels, from top to bottom: Basal, mid and apex-mid. Columns correspond to the instants of time, from left to right: end of the diastole ED, end of the systole ES and intermediate time between ED and ES.

270 distance. The method achieves accurate correspondences between both modalities
 271 with an average Dice score higher than 0.8, a level that could be clinically
 272 acceptable. However, a registration method can be useless if there are too
 273 many foldings in the deformation field, even for cases of good match. Hence,
 274 regularity of the deformation field, for the whole dataset, was evaluated by
 275 computing the number of voxels for which the determinant of the Jacobian is
 276 non-positive. This analysis showed only $0.2 \pm 0.3\%$ of the voxels exhibited such
 277 values. In addition, registration with the elastix [31] software corresponded to
 278 the nonrigid B-spline method [35,34], which has been described to robustly
 279 operate in similar problems [32,33].

280 In addition, the benefit of this method has been evaluated by computing
 281 the Dice Score and the Hausdorff distance at each step of the method to see

Table 1 Spatial registration performance, for healthy and pathological groups, by computing the Dice score and the Hausdorff distance

Measure	Healthy	Pathological
Dice Score	0.88 ± 0.03	0.83 ± 0.08
Hausdorff distance (mm)	12.02 ± 1.36	15.20 ± 2.93

**Fig. 5** Boxplot that shows the minimum and maximum values for a) Dice Score and b) Hausdorff distance computed in the healthy and pathological datasets

282 the contribution of the registration step in the saliency space. The results are
 283 presented in Table 2. Columns show the results about the type of transforma-
 284 tions applied in the saliency space. The first column represents the comparison
 285 of the LV surfaces without performing any transformation, i.e, the original LV
 286 surfaces compared between them. The remaining columns are then results of
 287 the initial, affine and non-rigid transformations applied to the salient volumes.
 288 Note how, the Dice Score value passed from 0.40 to 0.76 after applying the
 289 initial rigid transformation and then, the registration performance improved
 290 to 0.88, when the final stage, non-rigid registration, was performed. The same
 291 observations can be made for the Hausdorff distance, in which a value of
 292 13.01 mm was obtained after applying the initial registration, while a value of
 293 12.02 mm was estimated at the final stage.

Table 2 Spatial registration performance in each transformation: without any transformation (without), initial registration and final registration (affine and non-rigid), using the healthy dataset

Measure	Transformation			
	Without	Initial	Affine	Nonrigid
Dice Score	0.40 ± 0.13	0.76 ± 0.7	0.80 ± 0.05	0.88 ± 0.03
Hausdorff distance (mm)	15.30 ± 13.40	13.01 ± 0.13	12.89 ± 0.13	12.02 ± 1.36

Table 3 Spatial registration performance in the intensity space, for healthy and pathological groups, by computing the Dice score and the Hausdorff distance

Measure	Healthy	Pathological
Dice Score	0.77±0.05	0.79 ± 0.08
Hausdorff distance (mm)	19.34 ± 3.67	19.32 ± 4.04

294 Moreover, two additional experiments to emphasize the advantage of the
 295 method were performed. The first experiment consisted of aligning the inten-
 296 sity images using the same process computed for the salient volumes. The
 297 results are presented in Table 3, showing that the Dice Score measure was
 298 of 0.77 for 15 healthy cases and 0.79 for pathological cases, in comparison
 299 with the presented method, 0.88 and 0.83 for healthy and pathological sub-
 300 jects, respectively. In a similar way, the Hausdorff distance results were of
 301 19.34 mm and 19.32 mm for healthy and pathological subjects, while 12.02 m
 302 and 15.20 m for the presented strategy. These results highlight the advantage
 303 of using the saliency space to align the modalities. The second experiment con-
 304 sisted of adding Gaussian noise (with variance of 0.02) to the intensity images
 305 and after applying the registration in the saliency space. **For this experiment,**
 306 **a subset composed by five randomly selected healthy subjects was tested, re-**
 307 **porting a lower value of the Dice score and Hausdorff distance about 10% with**
 308 **respect to the results shown in Table 1.** These results suggest the saliency in
 309 echocardiography is affected by the noise, due to the fact that cardiac struc-
 310 tures can not be well recognized by fuzzy edges. This could be mitigated by
 311 performing a robust 3D denoising algorithm that improves the image quality
 312 in echocardiography.

313 As mentioned in the introduction, this paper is substantially different to the
 314 work published in [30], since a more detailed evaluation was performed and
 315 a larger dataset was used. **In addition,** the Dice score was computed for the
 316 resulting aligned LV surfaces from pathological subjects using the registration
 317 strategy described in that published work. **A Dice score of 0.78 was reported**
 318 **in that published work, while the presented method outperforms such work**
 319 **with a Dice score of 0.83, about 7%..** The advantages from this new work is
 320 the use of a 3D saliency, which is applied to each modality and the initial reg-
 321 istration. Unlike the previous work, which was performed using a 2D approach
 322 and without any initial alignment.

323 4 Conclusions

324 A novel 3D multimodal registration method was proposed. This strategy in-
 325 cludes the temporal information of the heart to obtain a common space of
 326 reference based on a saliency measure, where both modalities are aligned.
 327 The method has been tested on 15 healthy cases and 3 patients with car-
 328 diomyopathies. The evaluation has been realized by a visual and qualitative

way and by a quantitative strategy using Dice Score and 3D Hausdorff measures. Results have shown an interest of this method based on registration in saliency space by comparison to a registration approach based only on intensity. In addition, the results show an improvement when the initial rigid registration step results are compared with the results obtained at the final stage by using the saliency. Results have shown a good alignment between cMRI and 3DUS+t, even if the method has to be evaluated in a quantitative way on a large database. Future research will focus on improving the 3DUS image quality to obtain more reliable region of interest of the left ventricle. In addition, a rigid transformation between the modalities in the saliency space will be explored to study the effects of the heart deformation by our algorithm. The presented strategy will be tested with a larger dataset of healthy and pathological subjects and will be compared with other methods of the literature.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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