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# Establishing spatial correspondence for the analysis of images from highly deforming anatomy*

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*Abstract*— **This invited presentation summarizes recent advances in the incorporation of knowledge of the geometry, tissue mechanical properties and imaging characteristics in establishing spatial correspondence between multiple images of highly deforming, soft tissue structures. Spatial correspondence is used to aid diagnosis and in the extraction of quantitative parameters for disease detection, monitoring disease progression and assessing therapeutic response. The work is illustrated through clinical examples of multi-modal imaging of the breast, assessment of small bowel motility and polyp detection in the large bowel.**

## I. INTRODUCTION

Imaging of very soft and highly mobile organs, such as the breast and the bowel, remains a challenge when images are combined for screening applications and diagnosis, used for quantitative analysis for diagnosis and staging, and used to guide interventions. Strategies are required to compensate for deformation and motion and establish spatial correspondence between different acquisitions. This paper describes our recent progress in establishing spatial correspondence between X-ray mammograms and MR imaging for breast cancer diagnosis, the analysis of dynamic MRI for the study and staging of Crohn's disease and combining prone and supine CT scans for polyp detection using CT colonography. In all three applications spatial correspondence is achieved by matching using image intensities in the reconstructed images but in each case the transformation model used is informed by knowledge of the allowable tissue deformations and the constraints of the imaging systems used.

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## II. SPATIAL CORRESPONDENCE BETWEEN X-RAY AND MR IMAGES OF THE BREAST

### A. Clinical Motivation

Dynamic contrast enhanced MRI is indicated in younger women of high risk of developing breast cancer, those with dense breasts and in order to assist diagnosis in difficult cases [1]. Inevitable these women will have had an X-ray mammogram and a common but difficult task for the radiologist is to establish correspondence between the two imaging modalities. This is particularly important as there is a relatively high rate of false positive enhanced regions in breast MRI. A suitable method of establishing spatial correspondence would allow the radiologist to match a particular MR enhancing region with the appearance of the corresponding region in X-ray mammography, thus potentially reducing false positives and increasing confidence in true positives.

### B. Method

Our method, described more fully in [2], comprises the following steps: segmentation of fat, skin, chest wall and pectoral muscle and fibroglandular tissue from MRI; building a meshed model of the breast; deforming the mesh using an affine transformation, and more recently using a biomechanical model based on appropriate boundary conditions [3]; simulation of an X-ray mammogram from this deformed model and iterating trial transformations until the simulated X-ray mammogram matches the distribution of image intensities in the real X-ray mammogram. From this match a point or region on the MRI can be projected on to the X-ray image.

### C. Validation

Fifty-seven lesions from MRI and cranio-caudal (CC) and medio-lateral oblique (MLO) X-ray mammograms of 49 patients were annotated by our clinical partners at Nijmegen, yielding 113 registration tests. Registration was undertaken using an affine transformation model. The mean distance between the centers of the annotated regions was 13.1mm. For cranio-caudal X-ray mammogram views of 5 patients this process was repeated with the biomechanical model based deformation and the distance between the annotated region centers reduced from 13.0 mm +/- 7.1 for the affine transformation to 7.6 mm +/- 2.4 mm for the non-rigid deformation. This is sufficient for clinic

al utility in locating MR enhancing lesions in an X-ray mammogram.

### D. Conclusion

We have demonstrated a method for establishing correspondence between 2D projection X-ray mammograms with breast compressed and MRI with the patient supine and breast pendulous. The accuracy is sufficient for most diagnostic applications. This application demonstrates how a model of 3D breast anatomy coupled with an appropriate imager model and tissue deformation model can achieve clinically useful spatial correspondence between images from different modalities of a highly deformable organ.

## I. Analysis of bowel motility in Crohn's Disease

### A. Clinical Motivation

Dynamic MRI of the small bowel is an established investigation in the clinical management of enteric disorders. Quantitative evaluation of bowel motility has application in assessing segmental diseases and response to therapy in Crohn's disease as well as the diagnosis or follow-up of other chronic intestinal motility disorders. Quantitative evaluation of motility is complicated by the rapid motion of the bowel in 3D. In a typical clinical protocol, using our facilities, MRI is limited to between 0.65 to 0.8 seconds per frame at an in-plane resolution of between 0.8 mm and 0.9 mm, with slice thicknesses of 10 mm or more. This poses challenges for registration based motility analysis, yet imaging biomarkers of disease severity and therapy assessment require such quantitative measures.

### B. Method

Our groups have proposed a novel method for extracting reproducible and sensitive measures of bowel motility [4]. The key to our analysis is a 2D in-plane intensity-based non-rigid registration. Intensity changes arise from in-plane motion, through-plane motion and flow. We formulate the joint registration and modeling of intensity changes by minimizing the following cost function with respect to $u_x$, $u_y$ and $c$:

$$C(u_x, u_y, c) = SSD(u_x, u_y, c) + R(u_x, u_y, c)$$

The first term (SSD) is the sum-of-squared-differences between the reference image and the images obtained after registration and application of the model of intensity changes; the quantities $u_x$, $u_y$ are the displacements in-plane and the quantity $c$ is a model of all intensity changes that are not due to in-plane motion.

$R(u_x, u_y, c)$ is a regularization term imposing spatial smoothness on $u_x$, $u_y$, and $c$ based on their second-order spatial derivatives.

Minimising $C$ with respect to $(u_x, u_y, c)$ is a non-linear least squares optimization but is linearized at each iteration using a generalized version of the optical flow equation.

A measure of bowel motility is then computed as the standard deviation over time of the Jacobian determinant of the displacement fields (in 2D) and this is expected to reflect the amplitude of bowel contractions. For measurements taken over sufficient time the peak frequency of contractions may be estimated from the Fourier transform of the Jacobian determinant. A final measure of the bowel motility is given by the coefficient of variation of the estimate of $c$. More details of the mathematical development can be found in [4].

### C. Validation

The method has been validated on simulated data and tested on images from 5 patients. In the clinical study 50 bowel regions were graded by 2 expert observers into 4 grades or classes from normal motility to stationary and the standard deviation of the Jacobian gave 65% correct classification and 93% within one class tolerance, the coefficient of variation of $c$ gave 58% correct classification and 86% with one class tolerance, and the peak frequency of contractions gave 43% correct and 72% with one class tolerance. Agreement of automated estimates of in-plane displacements $(u_x, u_y)$ with observer values where comparable with inter-observer variability.

### D. Conclusions

Preliminary results from modeling intensity changes due to through-plane motion combined with non-rigid in-plane registration demonstrates automated assessment of small bowel motility that is as accurate as that obtained from observer studies. Further studies on significantly larger numbers of patients are planned to validate these methods as biomarkers of small bowel disease and its progression.

## II. Combining prone and supine CT scans for polyp detection using CT colonography

### A. Clinical motivation

Computed tomographic (CT) colonography is a technique for detecting bowel cancer or potentially precancerous polyps. CT scanning is combined with three-dimensional (3D) image reconstruction to produce a virtual endoluminal representation similar to optical colonoscopy. CT data are acquired with the bowel cleansed and insufflated with gas and the patient in both prone and supine positions. Residual fecal material can mimic the appearances of a polyp but such material is likely to move between the two acquisitions, a polyp will not. Radiologists visually match endoluminal locations between the two acquisitions in order to determine whether apparent pathology is real or not. This process is hindered by the fact that the colon, essentially a long tube, can undergo considerable deformation between acquisitions making it difficult to establish spatial correspondence between the two views. Different locations along the colon are difficult to distinguish from local anatomical features alone.

### B. Method

We have developed a robust and accurate method to automatically establish spatial correspondence between prone and supine intra-luminal colonic surfaces after surface parameterization from segmentations of CT colonography

images [5]. The complexity of the registration task is reduced from a 3D to a 2D problem by mapping the surfaces extracted from prone and supine CT colonography onto a cylindrical parameterization. This is done by segmenting the inner luminal surface of the colon [6], topological correction to remove segmentation errors, followed by production of a surface mesh using the marching cubes algorithm. The anus and caecum are identified and nodes removed resulting in a genus 1 surface. A 2D parameterization or conformal mapping of this surface is achieved using the Ricci flow method and Loop's subdivision [7]. Each location on this 2D parameterization is labeled with the shape index of the original surface.

This 2D representation represents a regular cylinder. The long axis corresponds approximately to the colon center line and the perpendicular axis to rotation around the cylinder surface repeating every 360 degrees. This 2D representation is obtained for both the prone and the supine CT colonography scans. A non-rigid 2D intensity based cylindrical registration was then performed between these two surfaces. The similarity metric used was the sum of square of differences (SSD) of the shape index and the transformation model used was standard 2D cubic B-Spline free form deformations defined on a regular array [8, 9]. A coarse-to-fine optimization strategy was used.

In order to deal with incompletely distended colons, common in clinical practice, the algorithm was modified to include user identification of the beginning and end of any collapse and this region was then excluded from computation of surface similarity.

We have also proposed a landmark-based initialization method to automatically detect folds using a graph cut method applied to a metric based on surface curvatures [10]. Shape index difference between pairs of images in the prone and supine position is used, along with additional neighborhood information enforcing geometric constraints based on angular and centerline displacement. A Markov Random Field model is used to calculate the maximum a posteriori fold labeling assignment.

### *C. Validation*

The method has been applied to a set of 13 sets of prone and supine CT colonography, consisting of 8 fully distended cases and 5 cases exhibiting multiple colonic collapses. Each study had one visible polyp. For the purposes of image registration the region around the polyp was masked and had no influence on the registration. All polyps present were well aligned, with a mean registration error of 5.7 mm +/- 3.4 mm.

An additional set of 1175 reference points on haustral folds spread over the full endoluminal colon surfaces resulted in an error of 7.7 (67.4) mm. Here, 82% of folds were aligned correctly after registration with a further 15% mis-registered by just one fold.

The landmark based initialization has been evaluated using cases with and without local colonic collapse with accuracies of 88.5% and 83.1% respectively. Moreover, it has also been shown to improve existing surface-based prone-supine registration algorithms by providing an initialization, increasing accuracy by 20.6% in the case of colonic collapse.

### *D. Conclusions*

The algorithm has now undergone significant clinical evaluation on 49 cases with 66 detected polyps with results to be reported elsewhere. This work demonstrates that a representation that considers the geometric constraint of the organ, in this case a cylinder representing the hollow tube of the colon, coupled with surface curvature measures can provide a robust and accurate means of aligning image data from a highly deforming, flexible structure.

## III. DISCUSSION

These three examples illustrate how combining:

1. knowledge of the overall geometry of an organ,
2. constraints on how tissue comprising that organ can deform, and
3. the imaging characteristics of the different imaging devices

can provide robust algorithms for establishing spatial correspondence in screening, diagnosis and treatment monitoring in difficult registration applications involving imaging of very mobile soft tissue structures.

In these applications we are not seeking registration accuracy corresponding to the spatial resolution of the imaging devices but spatial correspondence within a tolerance that is determined by the needs of the clinical application, i.e. approximately 10mm for the breast and colon and sufficient to allow derivation of quantitative measures of motility for the small bowel. Each application has been driven by clinical need and each is now undergoing large-scale clinical evaluation.

We are now developing ways to apply these methods to align pre-procedure image-derived information with laparoscopy and endoscopy. Future work includes relocating the same tissue when monitoring suspicious regions over extended time intervals (months or years) and establishing spatial correspondence between pre-operative image-derived information and emerging optical methods for in-vivo microscopy.

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