Non-rigid Free-Form 2D-3D Registration Using A B-spline-based Statistical Deformation Model

Weimin Yu^a, Moritz Tannast^b, Guoyan Zheng^{a,*}

^a*Institute for Surgical Technology and Biomechanics, University of Bern, Switzerland*

^b*Department of Orthopaedic Surgery, Inselspital, University of Bern, Switzerland*

Abstract

This paper presents a non-rigid free-form 2D-3D registration approach using a B-spline-based statistical deformation model (SDM). In our approach the B-spline-based SDM is first constructed from a set of training data using a non-rigid registration algorithm based on B-spline free-form deformation to encode *a priori* information about the underlying anatomy. A novel intensity-based non-rigid 2D-3D registration algorithm is then presented to iteratively fit the 3D B-spline-based SDM to the 2D X-ray images of an unseen subject, which requires a computationally expensive inversion of the instantiated deformation in each iteration. In this paper, we propose to solve this challenge with a fast 3D B-spline pseudo-inversion algorithm that is implemented on graphics processing unit (GPU). Comprehensive experiments on simulated images of patient data sets, on calibrated C-arm and on X-ray images of cadaveric femurs are designed and conducted to evaluate the performance of the proposed approach. The experimental results demonstrate the efficacy of the present approach.

Keywords: Free-form deformation, 2D-3D registration, pseudo inversion, GPU, Proximal femur

1. Introduction

Total Hip Arthroplasty (THA) has high social-economic impact. In developed countries including South Korea and Japan, more than 1.1 million

*Corresponding author. Tel.: +41-31-6315956 (Guoyan Zheng)

Email address: guoyan.zheng@ieee.org, guoyan.zheng@gmail.com
(Guoyan Zheng)

THAs were operated in 2006 (Kiefer, 2007). Among them, more than 650000 hip joint replacements and hip revision surgeries were performed in the European Union and USA contributed another 420000 hip joint arthroplasties (Kiefer, 2007).

Meticulous pre-operative planning and templating was advocated as an integral part of THA and is still an indispensable part of the surgical procedure. Accurate and reliable preoperative templating is essential in contemporary THA as it aids the surgeon in the selection of appropriate implant geometry, size, and position. This is especially true for a cementless THA as the endosteal fit of the femoral component is a major factor determining load transfer and, consequently, periprosthetic bone remodeling. Accurate metaphyseal stem fit is essential to reduce micromotion at the implant bone interface, and to minimize stress-shielding (Decking et al., 2006). Several studies have shown that femoral fit predicts not only radiographic changes following THA (Decking et al., 2006), but also affects clinical results in terms of implant survival (Aldinger et al., 2009). Although two-dimensional (2D) plain radiographs are the standard imaging means that are widely used in planning THA, several studies have demonstrated that radiographic assessment of femoral canal shape and geometry has limited reliability (Hayashi et al., 2015; Lecerf et al., 2009). A recent development was the introduction of computed tomography (CT) for 3-dimensional (3D) THA planning.

In comparison with plain radiograph, CT-based 3D planning of THA offers several advantages (Sariali et al., 2012; Huppertz et al., 2011). More specifically, CT has the benefits of avoiding errors resulting from magnification and inaccurate patient positioning. Additional benefits include the assessment in the axial plane, replacement of 2D projections with 3D data, and the availability of information on bone quality including accurate differentiation between cortical and cancellous bone. A randomized comparison between a 3D CT-based planning and a 2D plain radiograph based templating for THA showed that the prediction rate for the stem and the cup sizes for the 3D CT-based planning is two times more accurate than that for the 2D plain radiograph based templating (Sariali et al., 2012). The concern on 3D CT-based planning of THA, however, lies in the increase of radiation dosage to the patient (Huppertz et al., 2011; Sodickson et al., 2009) and the associated CT acquisition cost. An alternative is to reconstruct a patient-specific 3D volume data from 2D x-rays.

Depending on the output, 2D-3D reconstruction methods can be largely classified into two categories: 3D surface model reconstruction methods (Baka

et al., 2011; Fleute and Laval, 1998; Le Bras et al., 2004; Mitton et al., 2000; Zheng et al., 2009; Zheng, 2010b) and 3D volume reconstruction methods (Ahmad et al., 2010; Ehlke et al., 2013; Sadowsky et al., 2007; Whitmarsh et al., 2011; Yao and Taylor, 2003; Zheng, 2011; Lucas et al., 2012). The methods in the former category compute 3D patient-specific surface models from one or multiple 2D X-ray images. No intensity information or information about cortical bone is available. The reconstructed surface models may be used to plan cup component in THA as shown in (Schumann et al., 2015) or measure pelvis and THA acetabular component orientations as done by Zheng (2010b), but not for planning cementless stem component due to the missing information about proximal femur morphology and the intramedullary anatomy (Schumann et al., 2015).

The methods in the second category generate 3D patient-specific volumes from one or more X-ray images. Depending on the imaging device used to acquire the X-ray images, the methods in this category can be further classified into two subcategories: dual-energy X-ray absorptiometry (DXA) image based 2D-3D intensity volume reconstruction methods (Ahmad et al., 2010; Whitmarsh et al., 2011) and C-arm/plain X-ray radiograph-based 2D-3D intensity volume reconstruction methods (Ehlke et al., 2013; Sadowsky et al., 2007; Yao and Taylor, 2003; Zheng, 2011). With an orthographic camera model, a DXA image can be approximated by an isometric projection, removing the necessity for camera calibration (Whitmarsh et al., 2011). Thus, while the exact position of the scanned subject cannot be recovered, it is possible to obtain a reasonably accurate intensity volume reconstruction from a single DXA image. In contrast, the imaging geometry of a conventional C-arm/X-ray radiograph imaging device is usually described by a pin-hole perspective camera model, which means that with a single image it is difficult to separate the size change from the depth change (Zheng, 2010b). Thus, except for certain specific applications when objects with known sizes are available, in general it is difficult to reconstruct a 3D volume with a reasonably accurate estimation of the size information from a single C-arm/X-ray image. Two or more C-arm/X-ray images are required.

When two or more C-arm/X-ray images are available, Yao and Taylor (2003) and Sadowsky et al. (2007) proposed an iterative registration process to estimate the pose, scale and modes of variation of a tetrahedral meshes-based Statistical Shape and Intensity Model (SSIM) by minimizing the difference between the simulated Digitally Reconstructed Radiographs (DRRs) and the real X-ray images. Mutual information was used as the similarity

measure. With leave-one-out tests, an average registration error of 2.0 mm was reported by Sadowsky et al. (2007) but no information about computation time is described. This algorithm was recently accelerated with a GPU-algorithm for fast rendering of tetrahedral meshes with higher-order polynomial density functions (Ehlke et al., 2013).

Zheng (2011) proposed to reconstruct a patient-specific 3D volume by matching independent shape and appearance models that were learned from a set of training data to a limited number of C-arm/X-ray images. An intensity-based nonrigid 2D-3D registration algorithm was proposed to deformably fit the learned models to the input images. The fitting was conducted iteratively by minimizing the dissimilarity between the input images and the associated DRRs together with regularization terms encoding the strain energy of the forward deformation and the smoothness of the inverse deformation. It took about 15 minutes to finish one reconstruction when the algorithm was implemented with CPU computation without performance optimization. When two C-arm images were used, a mean reconstruction accuracy of 1.5 mm was reported by Zheng (2011). The mean reconstruction accuracy was changed to 1.4 mm when two calibrated X-ray images were used as the input.

In this paper, we propose a novel non-rigid free-form 2D-3D registration approach for a personalized reconstruction of the proximal femur from a limited number (e.g., 2) of 2D X-ray images. In comparison with previous work, our contributions are as follows:

- Unlike existing approaches, where statistical shape and appearance models (Sadowsky et al., 2007; Ahmad et al., 2010; Zheng, 2011; Whitmarsh et al., 2011) are used, we propose to use a B-spline-based statistical deformation model (SDM) introduced by Rueckert et al. (2001) to account for the mean and variability of the known deformations and thus encode *a priori* information about the underlying anatomy. Although a B-spline-based SDM has been used in various image computing tasks such as temporal subtraction of thorax radiographic images (Loeckx et al., 2003), ultrasound image-based shape instantiation (Barratt et al., 2008), and brain image registration (Rueckert et al., 2001; Pszczolkowski et al., 2012; Onofrey et al., 2015), to the best knowledge of the authors, this is the first time to use it in a 2D-3D registration scheme. The B-spline-based SDM used in our study has the advantages of constraining the 2D-3D registration procedure to produce only statis-

tically likely types of warps and of reducing the number of parameters to optimize.

- We develop and validate a fast 3D B-spline pseudo-inversion algorithm that is required in the iterative registration of the 3D B-spline-based SDM to the 2D X-ray images. In comparison with state-of-the-art 3D B-spline inversion algorithms (e.g., the one implemented in the registration toolbox 'elastix' (Klein et al., 2010; Metz et al., 2011)), which are usually done via non-rigid image registration, our 3D B-spline pseudo-inversion algorithm as implemented on graphics processing unit (GPU) achieves equivalent accuracy but is more than 100 times faster than the image registration based algorithm (Metz et al., 2011).
- We conduct comprehensive experiments for a thorough investigation of our approach.
- We evaluate not only the volume reconstruction accuracy but also the cortical bone region reconstruction accuracy, which is important for stem planning in cementless THA.

A preliminary version of this paper was reported in (Zheng and Yu, 2015) and here we extend it with detailed derivation and comprehensive experiments. The rest of the paper is arranged as follows. Section 2 presents the materials and methods. Experimental results are presented in Section 3, followed by discussions and conclusions in Section 4.

2. Materials and Methods

Our non-rigid free-from 2D-3D registration approach consists of two processes as shown in Fig. 1: the training process, where the B-spline-based SDM will be constructed from a set of training images, and the reconstruction process, where given X-ray images of an unseen subject, we will derive a patient-specific volume by non-rigidly matching the SDM to the input images. Note that the training process needs to be performed only once in order to be able to statistically register X-ray images of any unseen subject. Below details about each process will be given.

Figure 1: The proposed non-rigid free-form 2D-3D registration approach.

2.1. Training process

Following the idea introduced by Rueckert et al. (2001); Frangi et al. (2002), we construct the B-spline-based SDM from CT data of 40 left cadaveric proximal femurs based on a two-stage procedure. More specifically, in the first stage, we randomly chose one of the proximal femur from this given training population as the reference volume $\mathbf{V}_0^{1st}$. All other volumes $\{\mathbf{V}_i^{1st}, i = 1, \dots, 39\}$ were aligned to this reference volume with similarity registrations. We then applied the B-spline-based free-form deformation (FFD) algorithm (Rueckert et al., 1999) as implemented in the registration toolbox 'elastix' (Klein et al., 2010) to establish correspondences between the reference volume and each one of the 39 floating volumes. Each time, the output from the B-spline-based FFD algorithm is a local displacement field expressed as the 3D tensor product of the 1D cubic B-spline coefficients (Rueckert et al., 1999):

$$\mathbf{T}_i^{FFD}(\mathbf{x}) = \sum_{r=0}^3 \sum_{s=0}^3 \sum_{t=0}^3 B_r(u)B_s(v)B_t(w)\mathbf{c}_{l+r,m+s,n+t} \quad (1)$$

where $\mathbf{c}$ denotes the B-splines coefficients for a number of control points that form a regular lattice size of $(L + 3) \times (M + 3) \times (N + 3)$; l, m, n are

Figure 2: The mean and the first two modes of variations of the B-spline-based SDM.

the indexes of the control points satisfying $-1 \leq l \leq (L + 1)$, $-1 \leq m \leq (M + 1)$, $-1 \leq n \leq (N + 1)$, and $0 \leq u, v, w < 1$ corresponds to the relative positions of $\mathbf{x}$ in lattice coordinates.

By concatenating $(L + 3) \times (M + 3) \times (N + 3)$ 3D **B-spline coefficients** for each local displacement field, we have 39 FFDs described as **B-spline coefficient** vectors $\mathbf{C}_1^{1st}, \dots, \mathbf{C}_{39}^{1st}$, where $\mathbf{C}_i^{1st} = \text{vec}(\mathbf{c}_1, \dots, \mathbf{c}_{(L+3) \times (M+3) \times (N+3)})$. Here we use the operator, vec , to represent **B-spline coefficient** vectorization, and the operator, vec^{-1} , as the inverse of vectorization. Similarly, we can create 39 non-rigidly deformed floating volumes $\{\mathbf{I}_i^{1st}, i = 1, \dots, 39\}$, where $\mathbf{I}_i^{1st}$ is a concatenation of gray values in the i th warped floating volume. From these data, we computed the average **B-spline coefficient** vector $\bar{\mathbf{C}}^{1st} = (39^{-1}) \cdot \sum_{i=1}^{39} \mathbf{C}_i^{1st}$ and the average intensity distribution $\bar{\mathbf{I}} = (40^{-1}) \cdot \sum_{i=0}^{39} \mathbf{I}_i^{1st}$, with $\mathbf{I}_0^{1st}$ standing for gray values of the reference data.

As introduced by Rueckert et al. (2001); Frangi et al. (2002), the purpose of the second stage is to remove the possible bias introduced by the reference volume selection. To achieve this goal, we applied the FFD generated from the average **B-spline coefficient** vector $\bar{\mathbf{C}}^{1st}$ to the reference volume $\mathbf{V}_0^{1st}$ to create a new volume $\mathbf{s}_0$ and assigned the average intensity distribution $\bar{\mathbf{I}}$ to this newly created volume. The new volume $\mathbf{s}_0$ was named as the atlas.

It was used as the new reference volume in the second stage and all other 40 proximal femur volumes were regarded as the floating volumes. The B-spline-based FFD algorithm was used again to establish the correspondences between the atlas and the other 40 floating volumes. We thus obtained a set of 40 new B-spline coefficient vectors $\{\mathbf{C}_i; i = 1, \dots, 40\}$. We could then construct the B-spline-based SDM as:

$$\begin{aligned}\mathbf{S}_C &= ((m-1)^{-1}) \cdot \sum_{i=1}^m (\mathbf{C}_i - \bar{\mathbf{C}})(\mathbf{C}_i - \bar{\mathbf{C}})^T \\ \bar{\mathbf{C}} &= (m^{-1}) \cdot \sum_{i=1}^m \mathbf{C}_i \\ \mathbf{P}_C &= (\mathbf{p}_C^1, \mathbf{p}_C^2, \dots); \quad \mathbf{S}_C \cdot \mathbf{p}_C^i = (\sigma_C^i)^2 \cdot \mathbf{p}_C^i \\ \mathbf{C} &= \bar{\mathbf{C}} + \sum_{k=1}^{M_C} \alpha_C^k \sigma_C^k \mathbf{p}_C^k\end{aligned}\tag{2}$$

where $m = 40$ is the number of training samples; $\bar{\mathbf{C}}$ and $\mathbf{S}_C$ are the average and the covariance matrix of the **B-spline coefficient** vectors, respectively; $\{(\sigma_C^i)^2\}$ and $\{\mathbf{p}_C^i\}$ are the descendingly ordered eigen values and associated eigen vectors, respectively; $\{\alpha_C^i\}$ are the model parameters; M_C is the cut-off points.

Fig. 2 shows the mean and the first two modes of variations of the SDM. Each instance of the SDM was generated by evaluating $\mathbf{I}_s = \bar{\mathbf{I}}(T^{FFD}(\mathbf{C}) \circ \mathbf{s}_0)$, where $T^{FFD}(\mathbf{C}) = \sum_{r=0}^3 \sum_{s=0}^3 \sum_{t=0}^3 B_r(u)B_s(v)B_t(w)vec^{-1}(\mathbf{C})$ is the FFD generated from the instantiated **B-spline coefficient** vector $\mathbf{C} = \bar{\mathbf{C}} + \alpha_C \sigma_C^i \mathbf{p}_C^i$, with $\alpha_C \in \{-3.0, -1.5, 0, 1.5, 3.0\}$ (Cootes et al., 1995) and $i \in \{1, 2\}$ corresponding to the first two modes.

2.2. Reconstruction process

For an unseen proximal femur, we assume that we have a set of $Q \geq 2$ X-ray images and that all images are calibrated and co-registered to a common coordinate system called $\mathbf{f}$. Given an initial estimation of the registration parameters, our algorithm iteratively generates an 3D image and update the parameter estimation by minimizing the dissimilarity between the input 2D X-ray images and the associated DRRs that are created from the instantiated 3D image.

3D image instantiation and alignment. The 3D image instantiation and alignment process is parametrized by two sets of parameters, i.e., the set of shape parameters $\mathbf{b} = (\alpha_C^1, \alpha_C^2, \dots, \alpha_C^{M_C})^T$ determining a forward FFD from the atlas $\mathbf{s}_0$ to an instantiated 3D image $\mathbf{s}$ and the set of parameters $\mathbf{a} = (\Lambda, \beta, \gamma, \theta, t_x, t_y, t_z)^T$ determining a similarity transformation from the space of the instantiated image $\mathbf{s}$ to the common coordinate system $\mathbf{f}$, where

Figure 3: A schematic illustration of the backward warping.

Λ is the scaling parameter; β, γ, θ are rotational parameters and t_x, t_y, t_z are translational parameters. An instantiated 3D image that is aligned to the common coordinate system $\mathbf{f}$ is defined by following equation:

$$\bar{\mathbf{I}}(x_f(\mathbf{a}, \mathbf{b})) = \bar{\mathbf{I}}(\mathbf{A}(\mathbf{a}) \circ T^{FFD}(\mathbf{b}) \circ x_0) \quad (3)$$

where $\mathbf{A}(\mathbf{a})$ is the similarity transformation and $T^{FFD}(\mathbf{b})$ is the forward FFD.

Eq. 3 describes a forward warping. It is known that implementing this forward warping may result in holes in the aligned 3D image and a backward warping as follows should be used instead (see Fig. 3 for an illustration).

$$\bar{\mathbf{I}}(x_f^{q(i,j)}) = \bar{\mathbf{I}}(x_0) = \bar{\mathbf{I}}((T^{FFD}(\mathbf{b}))^{-1} \circ ((A(\mathbf{a}))^{-1} \circ x_f^{q(i,j)})) \quad (4)$$

where $x_f^{q(i,j)}$ is a sampled discrete point (see Fig. 3) along the back-projection ray of a pixel (i, j) in the q th input X-ray images.

It is straightforward to compute the inverse of the similarity transformation $\mathbf{A}(\mathbf{a})$. However, it is computationally expensive to compute the inverse of the forward FFD $T^{FFD}(\mathbf{b})$. In this paper, instead of computing the inverse of the forward FFD, we propose to compute a pseudo-inversion of the instantiated B-spline transformation following the idea introduced by Tristan and Arribas (2007). The computed pseudo-inversion B-spline coefficients then allow us to compute a backward FFD in order to warp the atlas to the instantiated volume $\mathbf{s}$. Below we will present details of our 3D extension to the

2D B-spline pseudo-inversion algorithm introduced by Tristan and Arribas (2007).

2.3. 3D B-spline pseudo-inversion algorithm

2.3.1. Notations

Before we present the details of our 3D B-spline pseudo-inversion algorithm, we introduce here the notations that will be used in our descriptions.

- $\{\mathbf{c}_{l,m,n}, l = -1 \sim L+1, m = -1 \sim M+1, n = -1 \sim N+1\}$: B-spline coefficients of an **instantiated** statistical deformation model.
- $\{\mathbf{d}_{l,m,n}^{\text{backward}}\}$: backward displacements at the positions of the B-spline control points.
- $\{(S_x, S_y, S_z)\}$: spacing of the B-spline lattice (unit: mm).
- $\{(O_x, O_y, O_z)\}$: origin of volume data.

2.3.2. Derivation

B-spline tensor product Given the volume space V with a compact support $\Omega = [O_x, X_{Upper}] \times [O_y, Y_{Upper}] \times [O_z, Z_{Upper}] \subset \mathbb{R}^3$, for any point $(x, y, z) \in \Omega$ and its deformed position $(x', y', z') \in \Omega$, we can calculate the displacement $(x' - x, y' - y, z' - z)$ via a B-spline tensor product as follows:

$$\begin{pmatrix} x' - x \\ y' - y \\ z' - z \end{pmatrix} = \begin{pmatrix} \sum_{r=0}^3 \sum_{s=0}^3 \sum_{t=0}^3 B_r(u) B_s(v) B_t(w) c_{l+r, m+s, n+t}^x \\ \sum_{r=0}^3 \sum_{s=0}^3 \sum_{t=0}^3 B_r(u) B_s(v) B_t(w) c_{l+r, m+s, n+t}^y \\ \sum_{r=0}^3 \sum_{s=0}^3 \sum_{t=0}^3 B_r(u) B_s(v) B_t(w) c_{l+r, m+s, n+t}^z \end{pmatrix} \quad (5)$$

where

$$\begin{cases} B_0(s) = \frac{-s^3+3s^2-3s+1}{6} \\ B_1(s) = \frac{3s^3-6s^2+4}{6} \\ B_2(s) = \frac{-3s^3+3s^2+3s+1}{6} \\ B_3(s) = \frac{s^3}{6} \end{cases} \quad (0 \leq s < 1) \quad (6)$$

are the B-spline basis functions, and

$$\begin{cases} l = \lfloor (x - O_x) / S_x \rfloor - 1 \\ m = \lfloor (y - O_y) / S_y \rfloor - 1 \\ n = \lfloor (z - O_z) / S_z \rfloor - 1 \end{cases} \quad \begin{cases} u = (x - O_x) / S_x - \lfloor (x - O_x) / S_x \rfloor \\ v = (y - O_y) / S_y - \lfloor (y - O_y) / S_y \rfloor \\ w = (z - O_z) / S_z - \lfloor (z - O_z) / S_z \rfloor \end{cases} \quad (7)$$

Here, the size of the B-spline lattice is calculated with

$$\begin{cases} L = \lfloor (X_{Upper} - O_x) / S_x \rfloor + 1 \\ M = \lfloor (Y_{Upper} - O_y) / S_y \rfloor + 1 \\ N = \lfloor (Z_{Upper} - O_z) / S_z \rfloor + 1 \end{cases} \quad (8)$$

B-spline pseudo-inversion At the positions of the B-spline control points, it can be derived that $u = v = w = 0$. Then, we have $B_3(u) = B_3(v) = B_3(w) = 0$, and the tensor product at the positions of these B-spline control points can be written as

$$\mathbf{d}_{l,m,n}^{\text{backward}} = \begin{pmatrix} \mathbf{d}_{l,m,n}^{\text{backward},x} \\ \mathbf{d}_{l,m,n}^{\text{backward},y} \\ \mathbf{d}_{l,m,n}^{\text{backward},z} \end{pmatrix} = \begin{pmatrix} \sum_{r=0}^2 \sum_{s=0}^2 \sum_{t=0}^2 a_r a_s a_t c_{l+r,m+s,n+t}^x \\ \sum_{r=0}^2 \sum_{s=0}^2 \sum_{t=0}^2 a_r a_s a_t c_{l+r,m+s,n+t}^y \\ \sum_{r=0}^2 \sum_{s=0}^2 \sum_{t=0}^2 a_r a_s a_t c_{l+r,m+s,n+t}^z \end{pmatrix} \quad (9)$$

where $a_0 = B_0(0) = \frac{1}{6}$, $a_1 = B_1(0) = \frac{2}{3}$ and $a_2 = B_2(0) = \frac{1}{6}$. Note that $\{\mathbf{d}_{l,m,n}^{\text{backward}}\}$ are derived using a fixed-point approach for inverting a deformation field (Chen et al., 2008). Please note that in the original work (Chen et al., 2008) the inversion is done for the complete volume, while in this study, we only need to compute the inverted displacement vectors at the positions of the B-spline control points.

Eq. 9 defines 3 sets of $(L + 3) \times (M + 3) \times (N + 3)$ equations with $3 \times (L + 3) \times (M + 3) \times (N + 3)$ unknowns. Each set of equations can be reformulated as a block-matrix style shown as below (without causing confusion, since now on we drop coordinate superscript).

$$\begin{pmatrix} a_1\Lambda & a_2\Lambda & 0 & 0 & \cdots & 0 & 0 \\ a_0\Lambda & a_1\Lambda & a_2\Lambda & 0 & \cdots & 0 & 0 \\ 0 & a_0\Lambda & a_1\Lambda & a_2\Lambda & \cdots & 0 & 0 \\ \vdots & \vdots & \ddots & \ddots & \ddots & \vdots & \vdots \\ 0 & 0 & 0 & 0 & \cdots & a_0\Lambda & a_1\Lambda \end{pmatrix}_{N+3} \begin{pmatrix} \mathbf{c}_{-1} \\ \mathbf{c}_0 \\ \mathbf{c}_1 \\ \vdots \\ \mathbf{c}_{N+1} \end{pmatrix} = \begin{pmatrix} \mathbf{d}_{-1}^{\text{backward}} \\ \mathbf{d}_0^{\text{backward}} \\ \mathbf{d}_1^{\text{backward}} \\ \vdots \\ \mathbf{d}_{N+1}^{\text{backward}} \end{pmatrix} \quad (10)$$

where Λ has the tridiagonal structure as shown in Eq. 11:

$$\Lambda = \begin{pmatrix} a_1\Lambda' & a_2\Lambda' & 0 & 0 & \cdots & 0 & 0 \\ a_0\Lambda' & a_1\Lambda' & a_2\Lambda' & 0 & \cdots & 0 & 0 \\ 0 & a_0\Lambda' & a_1\Lambda' & a_2\Lambda' & \cdots & 0 & 0 \\ \vdots & \vdots & \ddots & \ddots & \ddots & \vdots & \vdots \\ 0 & 0 & 0 & 0 & \cdots & a_0\Lambda' & a_1\Lambda' \end{pmatrix}_{M+3} \quad (11)$$

For a 3D case, the tridiagonal matrix Λ' in Eq. 11 is expressed as:

$$\Lambda' = \begin{pmatrix} a_1 & a_2 & 0 & 0 & \cdots & 0 & 0 \\ a_0 & a_1 & a_2 & 0 & \cdots & 0 & 0 \\ 0 & a_0 & a_1 & a_2 & \cdots & 0 & 0 \\ \vdots & \vdots & \ddots & \ddots & \ddots & \vdots & \vdots \\ 0 & 0 & 0 & 0 & \cdots & a_0 & a_1 \end{pmatrix}_{L+3} \quad (12)$$

Accordingly, for $n \sim (-1 : N + 1)$, $\mathbf{c}_n$ and $\mathbf{d}_n^{\text{backward}}$ also have nested vector structures which are described as below

$$\mathbf{c}_n = \begin{pmatrix} \mathbf{c}_{-1,n} \\ \mathbf{c}_{0,n} \\ \mathbf{c}_{1,n} \\ \vdots \\ \mathbf{c}_{M+1,n} \end{pmatrix} \quad \mathbf{d}_n^{\text{backward}} = \begin{pmatrix} \mathbf{d}_{-1,n}^{\text{backward}} \\ \mathbf{d}_{0,n}^{\text{backward}} \\ \mathbf{d}_{1,n}^{\text{backward}} \\ \vdots \\ \mathbf{d}_{M+1,n}^{\text{backward}} \end{pmatrix} \quad (13)$$

Similarly, for $m \sim (-1 : M + 1)$, $\mathbf{c}_{m,n}$ and $\mathbf{d}_{m,n}^{\text{backward}}$ are denoted as

$$\mathbf{c}_{m,n} = \begin{pmatrix} \mathbf{c}_{-1,m,n} \\ \mathbf{c}_{0,m,n} \\ \mathbf{c}_{1,m,n} \\ \vdots \\ \mathbf{c}_{L+1,m,n} \end{pmatrix} \quad \mathbf{d}_{m,n}^{\text{backward}} = \begin{pmatrix} \mathbf{d}_{-1,m,n}^{\text{backward}} \\ \mathbf{d}_{0,m,n}^{\text{backward}} \\ \mathbf{d}_{1,m,n}^{\text{backward}} \\ \vdots \\ \mathbf{d}_{L+1,m,n}^{\text{backward}} \end{pmatrix} \quad (14)$$

In summary, the size of the matrix Λ is $((L + 3) \times (M + 3)) \times ((L + 3) \times (M + 3))$, and the vectors $\mathbf{c}_n$ and $\mathbf{d}_n^{\text{backward}}$ have the length of $(L + 3) \times (M + 3)$. Furthermore, from Eq. 10, it can be derived that

$$a_0\Lambda\mathbf{c}_{n-1} + a_1\Lambda\mathbf{c}_n + a_2\Lambda\mathbf{c}_{n+1} = \mathbf{d}_n^{\text{backward}} \quad (-1 < n < N + 1) \quad (15)$$

Since for any two vectors A and B of the same length S , there exists the relation that $A = \sum \cdot B + \theta$ where $\sum$ is a $S \times S$ diagonal matrix and θ is a vector of the length S . Therefore, we can assume that

$$\mathbf{c}_{n+1} = \sum_n \mathbf{c}_n + \theta_n \quad (-2 \leq n \leq N+1) \quad (16)$$

where we extend the boundary valeus $\mathbf{c}_{-1}$ to $\mathbf{c}_{-2}$, and $\mathbf{c}_{N+1}$ to $\mathbf{c}_{N+2}$, i.e., we assume that $\mathbf{c}_{-2} = \mathbf{c}_{-1}$ and $\mathbf{c}_{N+2} = \mathbf{c}_{N+1}$.

Combining Eq. 15 and Eq. 16, we have

$$\begin{aligned} \left(\frac{a_1}{a_2} I + \sum_n \right) \mathbf{c}_n &= -\mathbf{c}_{n-1} + \left(\frac{1}{a_2} \Lambda^{-1} \mathbf{d}_n^{\text{backward}} - \theta_n \right) \\ \Rightarrow \mathbf{c}_n &= -\left(\frac{a_1}{a_2} I + \sum_n \right)^{-1} \mathbf{c}_{n-1} + \left(\frac{a_1}{a_2} I + \sum_n \right)^{-1} \left(\frac{1}{a_2} \Lambda^{-1} \mathbf{d}_n^{\text{backward}} - \theta_n \right) \end{aligned} \quad (17)$$

From Eq. 17, we can conclude that

$$\begin{cases} \sum_{n-1} = -\left(\frac{a_1}{a_2} I + \sum_n \right)^{-1} \\ \theta_{n-1} = \left(\frac{a_1}{a_2} I + \sum_n \right)^{-1} \left(\frac{1}{a_2} \Lambda^{-1} \mathbf{d}_n^{\text{backward}} - \theta_n \right) \end{cases} \quad (-1 \leq n \leq N+1) \quad (18)$$

As we assume $\mathbf{c}_{N+2} = \mathbf{c}_{N+1}$, then we have $\sum_{N+1} = \gamma_{N+1} \cdot I$ and $\theta_{N+1} = 0$, where $\gamma_{N+1} = 1$. Thus, recursively, we have:

$$\begin{cases} \sum_N = -\left(\frac{a_1}{a_2} I + \gamma_{N+1} \cdot I \right)^{-1} = -\frac{1}{a_1/a_2 + \gamma_{N+1}} I = \gamma_N \cdot I \\ \sum_{N-1} = -\left(\frac{a_1}{a_2} I + \sum_N \right)^{-1} = -\left(\frac{a_1}{a_2} I + \gamma_N \cdot I \right)^{-1} = -\frac{1}{a_1/a_2 + \gamma_N} I = \gamma_{N-1} \cdot I \\ \vdots \\ \sum_{-1} = -\left(\frac{a_1}{a_2} I + \sum_0 \right)^{-1} = -\left(\frac{a_1}{a_2} I + \gamma_0 \cdot I \right)^{-1} = -\frac{1}{a_1/a_2 + \gamma_0} I = \gamma_{-1} \cdot I \end{cases} \quad (19)$$

Accordingly, γ_n is recursively described as:

$$\begin{cases} \gamma_{n-1} = -\frac{1}{a_1/a_2 + \gamma_n} \quad (-1 \leq n \leq N+1) \\ \gamma_{N+1} = 1 \end{cases} \quad (20)$$

and

$$\begin{cases} \theta_{n-1} = \left(\frac{a_1}{a_2} I + \sum_n \right)^{-1} \left(\frac{1}{a_2} \Lambda^{-1} \mathbf{d}_n^{\text{backward}} - \theta_n \right) = -\gamma_{n-1} \left(\frac{1}{a_2} \Lambda^{-1} \mathbf{d}_n^{\text{backward}} - \theta_n \right) \\ \theta_{N+1} = 0 \end{cases} \quad (21)$$

Finally, Eq. 17, 18, 20 and 21 allow us to derive that

$$\mathbf{c}_n = \gamma_{n-1}\mathbf{c}_{n-1} + \theta_{n-1} \quad (-1 \leq n \leq N+1) \quad (22)$$

Since $\mathbf{c}_{-2} = \mathbf{c}_{-1}$ by extending the boundary along Z-axis, we have

$$\mathbf{c}_{-1} = \gamma_{-2}\mathbf{c}_{-2} + \theta_{-2} \Rightarrow \mathbf{c}_{-1} = \mathbf{c}_{-2} = \frac{\theta_{-2}}{1 - \gamma_{-2}} \quad (23)$$

With Eq. 20, 21, 22 and 23, we can calculate the backward B-spline coefficients for an instantiation of the statistical deformation model, and it facilitates to get the displacement at any position via 3D B-spline tensor product of the backward B-spline coefficients. To speed up the the computation of the 3D B-spline pseudo-inversion, we have implemented the algorithm on GPU with the Compute Unified Device Architecture (CUDA) programming environment.

2.4. Non-rigid free-form 2D-3D registration

Registration Criterion. We chose to use the robust dissimilarity measure introduced by Zheng (2010a) to compare the floating DRRs to the associated reference X-ray images. This robust dissimilarity measure is defined as:

$$\begin{aligned} E(\mathbf{a}, \mathbf{b}) = & \sum_{q=1}^Q [\lambda \sum_{i,j}^{I,J} D_{q;(i,j)}^2(\mathbf{a}, \mathbf{b}) + \\ & (1 - \lambda) \sum_{i,j}^{I,J} \frac{1}{\text{card}(N_{i,j}^r)} \sum_{(i',j') \in N_{i,j}^r} (D_{q;(i,j)}(\mathbf{a}, \mathbf{b}) - D_{q;(i',j')}(\mathbf{a}, \mathbf{b}))^2] \end{aligned} \quad (24)$$

where $I \times J$ is the size of each X-ray image; $D_q = \{D_{q;(i,j)}\}$ is the q th observed difference image; $N = \{N_{i,j}^r\}$ are the r th order neighborhood systems and $\text{card}(N_{i,j}^r)$ is the number of pixels in $N_{i,j}^r$. We refer interesting readers to Zheng (2010a) for the details about how the difference images are computed and about the details of above equation.

Optimization Strategy. Considering the least-squares form of Eq. 24, we decided to use Levenberg-Marquardt optimizer to minimize $E(\mathbf{a}, \mathbf{b})$. More specifically, the following two stages are executed until convergence.

- Similarity registration stage: The shape parameters are fixed to the current estimation $\mathbf{b}_t$ and the Levenberg-Marquardt optimizer is used to iteratively minimize the image dissimilarity energy $E(\mathbf{a}, \mathbf{b}_t)$ in order to obtain a new estimation of the similarity transformation parameters $\mathbf{a}_{t+1}$.
- Non-rigid registration stage: The similarity transformation parameters are fixed to $\mathbf{a}_{t+1}$ and the Levenberg-Marquardt optimizer is used again to iteratively estimate the new shape deformation parameters $\mathbf{b}_{t+1}$. At each iteration, following two steps are performed.
 - Step 1: Following the Levenberg-Marquardt optimizer, compute the gradient and the regularized Hessian of Eq. (5) with respect to the shape parameters, and then calculate an additive update $\Delta\mathbf{b}_t$ of the shape parameters to get a new estimation $\mathbf{b}_{t+1} = \mathbf{b}_t + \Delta\mathbf{b}_t$.
 - Step 2: Based on $\mathbf{b}_{t+1}$, we first instantiate the B-spline coefficient vector $\mathbf{C} = \bar{\mathbf{C}} + \sum_{k=1}^{M_C} \alpha_C^k \sigma_C^k \mathbf{p}_C^k$. We then compute its pseudo-inversion. Based on the inverted B-splines coefficients, we can compute a backward FFD, which will be used to warp the atlas to the instantiated image $\mathbf{s}$ to generate DRRs for the next iteration.

3. Experimental Results

The atlas has a resolution of $192 \times 128 \times 192$ voxels with a voxel size of $0.664 \times 0.664 \times 1.0mm^3$. The control point lattice has a size of $25 \times 18 \times 35$ points with a grid spacing of $6.0 \times 6.0 \times 6.0mm^3$. For all the registration experiments, the cut-off point M_C was empirically chosen to be 9. Shape parameters $\mathbf{b}$ were initialized to zeros and pose parameters $\mathbf{a}$ were initialized with anatomical landmark based registration. Implemented on a laptop with 2.5 GHz Intel Core i5 processor and Nvidia GeForce GT 750M graphics card, it took about 5-7 minutes to register the B-spline-based SDM to 2 X-ray images with a resolution of 768×576 pixels.

3.1. Evaluation metrics.

In our experiments, we used following metrics to evaluate the performance of the present approach.

**A patient's CT
cropped around the
proximal femur
region for
visualization purpose**

**Manually extracted
binary mask for
segmenting the overall
volume of the proximal
femur**

**Manually extracted
binary mask for
segmenting the cortical
bone region visualized in
5 2D axial slices together
with the outer surface
(transparent).**

Figure 4: An example of manual segmentation of a patients CT, from left to right: the original CT data, the segmented proximal femur volume, and the segmented cortical bone region visualized in five 2D axial slices.

- 3D dice coefficients (DC). It is a metric defined as follows (Dice, 1945): with L_1 being the binary segmentation obtained from the ground truth CT data and L_2 being the binary segmentation obtained from the reconstructed volume, DC is defined as $DC = 2|L_1 \cap L_2|/(|L_1| + |L_2|)$. The binary segmentation was manually done with commercial software Amira (www.vsg3d.com/amira). See Fig. 4, middle, for an example.
- 3D average surface distance (ASD). It is a metric defined as the average distance between points on the surface of a ground truth volume to the outer surface extracted from the binary segmentation of the reconstructed volume.
- 3D cortical bone region dice coefficients (CBRDC). It is a metric used to measure the cortical bone reconstruction quality. To calculate such a metric, we first manually segmented the cortical bone region from the ground truth CT data (see Fig. 4, right, for an example), which was regarded as the reference cortical bone region. Furthermore, we manually segment the volumetric atlas to get a binary mask of the cortical bone region. After the non-rigid free-form 2D-3D registration, we will obtain a deformation field between the volumetric atlas and the reference space of the 2D X-ray images. We can use the obtained deformation field to warp the binary mask of the cortical bone region of the volumetric atlas to get the reconstructed cortical bone region, which was then compared with the reference cortical bone region. CBRDC is calculated as the DC between these two binary masks.
- 3D cortical bone region ASD (CBRASD). It is a metric defined as the ASD between the inner cortical bone surfaces extracted from the two binary masks of the segmented cortical bone regions.

3.2. Pseudo-inversion validation experiment.

Due to the facts that no direct validation was conducted by Tristan and Arribas (2007) to validate the accuracy of the 2D B-spline pseudo-inversion algorithm and that we have developed and implemented a GPU-based 3D extension of the 2D pseudo-inversion algorithm, we designed this experiment to validate the accuracy of our 3D B-spline pseudo-inversion algorithm by comparing the backward FFD calculated from the results of our pseudo-inversion algorithm with the one computed by 'elastix' (Klein et al., 2010; Metz et al., 2011) via non-rigid image registration, which is regarded as

Table 1: Pseudo-inverse validation results where R_x , R_y , and R_z are correlation coefficients of the two backward FFDs along x , y , and z axis, respectively.

Quantity		#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	Average
R_x		0.993	0.997	0.998	0.994	0.991	0.997	0.995	0.997	0.998	0.997	0.996
R_y		0.996	0.997	0.997	0.996	0.996	0.997	0.997	0.997	0.997	0.996	0.997
R_z		0.998	0.995	0.993	0.998	0.998	0.995	0.993	0.995	0.993	0.994	0.995
$Mean_M$ (mm)		0.049	0.086	0.081	0.095	0.104	0.097	0.097	0.094	0.084	0.096	0.088
$Median_M$ (mm)		0.014	0.024	0.023	0.023	0.025	0.027	0.027	0.023	0.021	0.027	0.023
Computing	elastix	202	200	199	201	204	205	205	204	202	203	202.5
Time (s)	Ours	1.33	1.22	1.02	1.06	1.01	1.09	1.05	1.03	1.09	0.98	1.09

Table 2: Results of experiment on C-arm images of 10 cadaveric femurs.

Quantity		#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	Average
Mean (mm)		1.5	1.0	1.1	1.0	1.4	1.6	1.4	1.3	1.1	1.1	1.3
Median (mm)		1.2	0.7	0.8	0.8	1.1	1.4	1.2	1.1	0.9	0.9	1.0

the baseline algorithm. Please note that in 'elastix' a smaller grid spacing than the forward FFD is chosen for the inverse transform which prevents a direct comparison of the inverted B-splines coefficients generated by these two different methods (Metz et al., 2011). This experiment was conducted on the registration outputs of the first 10 proximal femurs in the second stage of the B-spline-based SDM construction. Correlation along each axis of the two backward FFDs, the mean and median magnitudes ($Mean_M$ and $Median_M$) of the difference vectors at all voxels, and the computing time are presented in Table 1. Based on the results presented in Table 1, it was found that our B-spline pseudo-inversion algorithm achieved a reasonably good accuracy but was more than 100 times faster than the baseline algorithm.

3.3. Experiment on C-arm images of 10 cadaveric femurs.

In this experiment, 10 cadaveric femurs (none of them was used in the SDM construction) were used. For each femur, we acquired two calibrated C-arm images around the proximal region. The reconstruction accuracies were evaluated by randomly digitizing dozens points from the surface of each femur using a tracked pointer and then computing the distances from those digitized points to the associated surface model which was segmented from the reconstructed volume. Mean and median reconstruction errors for each femur are presented in Table 2. The mean reconstruction errors range from 1.0 mm to 1.6mm and an average accuracy of 1.3 mm was found.

Figure 5: A reconstruction example and the color-coded error distribution when the surface model segmented from the reconstructed volume is compared with the ground truth (mean error = 0.9 mm and maximum error = 3.7 mm).

3.4. Experiment on X-ray images of 21 cadaveric femurs.

In this experiment, X-ray images of another 21 cadaveric femurs (again, none of them was used in the SDM construction) were used, where 5 of them were part of complete hips. For each femur, the ground truth surface models were either obtained with a CT-scan reconstruction method (for complete hips) or with a hand-held laser-scan reconstruction method (for others). The surface models segmented from the reconstructed volumes were then compared to the associated ground truth models to evaluate the reconstruction accuracies. A reconstruction example and the color-coded reconstruction error distribution are shown in Fig. 5. The errors of reconstructing volumes of all 21 femurs were presented in Fig. 6. Our approach could successfully reconstruct volumes of all 21 femurs. An average mean reconstruction accuracy of 1.16 mm was found, which was regarded as accurate enough for our clinical applications.

Figure 6: Errors of comparing surface models segmented from reconstructed volumes of all 21 femurs with the associated ground truth.

3.5. Experiment on simulated X-ray images of 20 femurs.

In this experiment, we will evaluate both the overall volume reconstruction accuracy as well as the cortical bone region reconstruction accuracy. To this end, anonymized CT data of 20 patients from a retrospective study investigating medium and long-term results after unilateral THA were used in this study. For each patient, CT data of the side without an implantation were used. The intra-slice resolutions of the CT data range from 0.55mm to 0.83mm and their inter-slice resolutions range from 1.7mm to 2.5mm. For each patients CT data, two DRRs are generated as the input for this experiment. In addition to estimating DC and ASD between the ground truth CT data and the reconstructed volume, we further calculated CBRASD and CBRDC to estimate the cortical bone reconstruction accuracy. The volume reconstruction errors and the cortical bone region reconstruction errors of the present approach are shown in Table 3. The mean ASD, the mean DC, the mean CBRASD and the mean CBRDC achieved by the present method are $1.0 \pm 0.2\text{mm}$, $95.0 \pm 1.3\%$, $0.9 \pm 0.2\text{mm}$ and $78.8 \pm 4.2\%$, respectively. Fig. 7 shows a comparison of the reconstructed volumes with the associated ground truth volumes. From this figure, one can clearly see that our approach accurately reconstruct the proximal femur morphology and the intramedullary anatomy.

Figure 7: Comparison of the reconstructed volumes with the associated ground volumes extracted from CT data. Top two rows: slice views of the ground truth volumes and the reconstructed volumes of three different patients; bottom row: surface models of the same three patients extracted from the reconstructed volumes with color-coded error distributions.

Table 3: Volume and cortical bone region reconstruction accuracy of our approach when evaluated on anonymized data of the 20 patients.

Metrics	$Mean \pm STD$	Median	Min	Max
ASD (mm)	1.0 ± 0.2	1.0	0.6	1.6
DC (%)	95.0 ± 1.3	94.2	91.1	95.9
CBRASD (mm)	0.9 ± 0.2	0.9	0.6	1.5
CBRDC (%)	78.8 ± 4.2	80.0	70.0	83.6

4. Discussions and Conclusion

In this paper, we proposed a non-rigid free-from 2D-3D registration approach using B-spline-based SDM and showed its application to a personalized reconstruction of 3D volumes of the proximal femur. The iterative registration of the B-spline-based SDM to the input X-ray images required a computationally expensive inversion of the instantiated deformation in each iteration. In this paper, we solved this challenge with a fast 3D B-spline pseudo-inversion algorithm that was implemented on GPU. The efficacy of the present 2D-3D reconstruction method was finally evaluated on calibrated C-arm and X-ray images of in total 31 cadaveric femurs, and on simulated X-ray images of 20 patients.

In comparison to the state of the art works on 2D-3D volume reconstruction (Ahmad et al., 2010; Ehlke et al., 2013; Sadowsky et al., 2007; Whitmarsh et al., 2011; Yao and Taylor, 2003; Zheng, 2011; Lucas et al., 2012), our approach has several advantages. For example, the shape model presented by Zheng (2011) was constructed on dense deformation fields while we constructed our SDM on sparse B-spline coefficient vectors, which required much less storage space. Furthermore, using the inverted B-spline coefficients to compute the backward FFD can be viewed as a smoothing alternative in which explicit regularization is achieved through B-spline approximation. Thus, no additional regularization is needed. Although it is difficult to compare the performance of different methods due to the fact that different data sets were used in different studies, both the method introduced by Zheng (2011) and the present approach have been evaluated on the same C-arm and X-ray images of 31 cadaveric femurs, which allows us to compare the performance. Specifically, an average reconstruction accuracy of 1.5 mm was reported by Zheng (2011) when two C-arm images were used as the input. In contrast, the present approach achieved an average

reconstruction accuracy of about 1.3 mm on the same data set. When two calibrated X-ray images were used as the input, an average reconstruction accuracy of 1.4mm was reported by Zheng (2011) while in this study our approach achieved an average reconstruction accuracy of about 1.2mm when evaluated on the same data set.

FFD is a popular algorithm for elastic image registration since its introduction (Rueckert et al., 1999). However, due to the unconstrained nature of the registration, FFD may introduce unrealistic deformations. Prior knowledge in the form of SDM in a registration scheme has been shown to function as an effective regularizer (Rueckert et al., 2001; Loeckx et al., 2003; Barratt et al., 2008; Pszczolkowski et al., 2012; Onofrey et al., 2015). Different from previous work on using SDM in a registration scheme, we introduced a fast and accurate 3D algorithm to find a B-spline transformation that approximates the inversion of a B-spline transformation instantiated from the SDM, which facilitates the application of SDM for non-rigid free-form 2D-3D registration.

Other potential applications of the present B-spline pseudo-inversion algorithm are for 3D-3D consistent image registration (Christensen and Johnson, 2001; Shen and Davatzikos, 2002; Ashburner, 2007; Vercauteren et al., 2009) and for adaptive radiation therapy (Chen et al., 2008; Yan et al., 2010; Vercauteren et al., 2013). Inverse consistent image registration methods strive to overcome the problems related to a non-unique correspondence between different image sets. For example, Christensen and Johnson (2001) used a symmetric similarity measure and deformation field inversion to achieve inverse consistency. Ashburner (2007) introduced an algorithm using exponentiated Lie algebra with computation of a deformation field and its inverse from a flow field to achieve a diffeomorphic image registration, and Vercauteren et al. (2009) used the log-Euclidean framework to implement inverse consistent image registration. Although inverse consistency is a desirable property, there exists other image registration algorithms which neither automatically generate the reverse field nor have proven to generate invertible deformation fields (Chen et al., 2008; Yan et al., 2010; Klein et al., 2010; Metz et al., 2011; Vercauteren et al., 2013). For these algorithms, in order to compute an inverse of the generated deformation field, heuristic approaches (Yan et al., 2010; Vercauteren et al., 2013) and iterative algorithm based on a fixed-point theory (Chen et al., 2008) have been reported. Our algorithm also used the fixed-point approach (Chen et al., 2008) to derive backward displacement vectors before computing a pseudo-inversion of an instantiated

B-spline transformation. Our algorithm differs from the algorithms introduced by Chen et al. (2008); Yan et al. (2010); Vercauteren et al. (2013) in the number of displacement vectors that need to be inverted and in the way to represent the backward deformation. More specifically, in (Chen et al., 2008; Yan et al., 2010; Vercauteren et al., 2013), the inversion was done at every voxel of the volume. In contrast, our algorithm only needs to compute the inverted displacement vectors at every point of the B-spline lattice, whose dimension is much smaller than the volume dimension. Considering the iterative characteristics of the algorithm introduced by Chen et al. (2008), such a reduction of the number of displacement vectors to be inverted significantly reduce the required computation time. Furthermore, representing the backward deformation as a B-spline transformation in our algorithm has the desired property that the resultant backward deformation field be smooth.

There exist other methods to compute a pseudo-inversion of a B-spline transformation. For example, Metz et al. (2011) reported a method to compute a pseudo-inversion of a B-spline transformation using non-rigid image registration (Klein et al., 2010). As demonstrated by our experimental results, to get a reasonable accurate pseudo-inversion of a given B-spline transformation, our algorithm is more than 100 times faster than the algorithm reported by Metz et al. (2011), which is a clear advantage.

In summary, we presented a non-rigid free-form 2D-3D registration approach for personalized reconstruction of 3D volumes of the proximal femur. Comprehensive evaluation demonstrated the efficacy of the present approach. In the future, we will investigate the application of the present approach to other anatomical structures.

5. Acknowledgements

The paper is partially supported by the Japanese-Swiss Science and Technology Cooperation Program and the Swiss National Science Foundation (SNSF) Project No. 205321_138009/1. M. Tannast received support from SNSF via Project No. PP00P3_144856.

Ahmad, O., Ramamurthi, K., Wilson, K., Engelke, K., Prince, R., Taylor, R., 2010. Volumetric dxa (vxa): A new method to extract 3d information from multiple in vivo dxa images. *J Bone Miner Res* 25 (12), 2744–2751.

Aldinger, P., Jung, A., Pritsch, M., Breusch, S., Thomsen, M., Ewerbeck, V., Parsch, D., 2009. Uncemented grit-blasted straight tapered titanium

stems in patients younger than fifty-five years of age. fifteen to twenty-year results. *J Bone Joint Surg Am* 91 (6), 1432–1439.

Ashburner, H., 2007. A fast diffeomorphic image registration algorithm. *Neuroimage* 38 (1), 95–113.

Baka, N., Kaptein, B., de Bruijne, M., van Walsum, T., Giphart, J., Niessen, W., Lelieveldt, B., 2011. 2d-3d shape reconstruction of the distal femur from stereo x-ray imaging using statistical shape models. *Med Image Anal* 15 (6), 840–850.

Barratt, D., Chan, C., Edwards, P., Penney, G., Slomczykowski, M., Carter, T., Hawkes, D., 2008. Instantiation and registration of statistical shape models of the femur and pelvis using 3d ultrasound imaging. *Med Image Anal.* 12 (3), 358–374.

Chen, M., Lu, W., Chen, Q., Ruchala, K., 2008. A simple fixed-point approach to invert a deformation field. *Med. Phys* 35, 81–88.

Christensen, G., Johnson, H., 2001. Consistent image registration. *IEEE Trans Med Imaging* 20 (7), 568–582.

Cootes, T.F., Taylor, C.J., Cooper, D.H., Graham, J., 1995. Active shape models - their training and application. *Comput Vis Image Underst* 61 (1), 38–59.

Decking, R., Puhl, W., Simon, U., Clase, L., 2006. Changes in strain distribution of loaded proximal femora caused by different types of cementless femoral stem. *Clin Biomech* 21 (5), 495–501.

Dice, L., 1945. Measures of the amount of ecologic association between species. *Ecology* 26 (3), 297–302.

Ehlke, M., Ramm, H. andLamecker, H., Hege, H., Zachow, S., 2013. Fast generation of virtual x-ray images for reconstruction of 3d anatomy. *IEEE Trans Vis Comput Graph* 19 (12), 2673–2682.

Fleute, M., Lavalle, S., 1998. Nonrigid 3d/2d registration of images using statistical models. In: *Proceedings of MICCAI 1998, LNCS 1496*. pp. 138–147.

Frangi, A., Rueckert, D., Schnabel, J., Niessen, W., 2002. Automatic Construction of Multiple-Object Three-Dimensional Statistical Shape Models: Application to Cardiac Modeling. *IEEE Trans Med Imaging* 21 (9), 1151-1166.

Hayashi, S., Fujishiro, T., Hashimoto, S., Kanzaki, N., Kuroda, R., Kurosaka, M., 2015. The contributing factor of tapered wedge stem alignment during mini-invasive total hip arthroplasty. *Journal of Orthopaedic Surgery and Research* 10 (52).

Huppertz, A., Radmer, S., Asbach, P., Juran, R., Schwenke, C., Diederichs, G., Hamm, B., Sparmann, M., 2011. Computed tomography for preoperative planning in minimal-invasive total hip arthroplasty: radiation exposure and cost analysis. *Eur J Radiol.* 78 (3), 406–413.

Kiefer, H., 2007. Differences and opportunities of tha in the usa, asia and europe. In: Chang, J.-D., Billau, K. (Eds.), *Proceedings of the 12th BIOLOX Symposium Seoul, Republic of Korea September 7–8, 2007*. Springer, Berlin, pp. 3–8.

Klein, S., Staring, M., Murphy, K., Viergever, M., Pluim, J., 2010. Elastix: a toolbox for intensity-based medical image registration. *IEEE Trans Med Imaging* 29 (1), 196–205.

Le Bras, A., Laporte, S., Bousson, V., Mitton, D., De Guise, J., Laredo, J., Skalli, W., 2004. 3d reconstruction of the proximal femur with low-dose digital stereoradiography. *Comput Aided Surg* 9 (3), 51–57.

Lecerf, G., Fessy, M., Philippot, R., Massin, P. and Giraud, F., Flecher, X., Girard, J., Mertl, P., Marchetti, E., Stindel, E., 2009. Femoral offset: anatomical concept, definition, assessment, implications for peroperative templating and hip arthroplasty. *Orthop Traumatol Surg Res* 95, 210–219.

Loeckx, D., Maes, F., Vandermeulen, D., Suetens, P., 2003. Temporal subtraction of thorax cr images using a statistical deformation mode. *IEEE Trans Med Imaging* 22 (11), 1490–1504.

Lucas, B., Otake, Y., Armand, M., Taylor, R., 2012. An active contour method for bone cement reconstruction from c-arm x-ray images. *IEEE Trans Med Imaging* 31 (4), 860–869.

- Metz, C.T., Klein, S., Schaap, M., van Walsum, T., Niessen, W.J., 2011. Nonrigid registration of dynamic medical imaging data using nD+t B-splines and a groupwise optimization approach. *Med Image Anal.* 15 (2), 238–249.
- Mitton, D., Landry, C., Vron, S., Skalli, W., Lavaste, F., De Guise, J., 2000. 3d reconstruction method from biplanar radiography using non-stereocorresponding points and elastic deformable meshes. *Med Biol Eng Comput.* 38 (2), 133–139.
- Onofrey, J., Papademetris, X., Staib, L., 2015. Low-dimensional non-rigid image registration using statistical deformation models from semi-supervised training data. *IEEE Trans Med Imaging* 34 (7), 1522 – 1532.
- Pszczolkowski, S., Pizarro, L., Guerrero, R., Rueckert, D., 2012. Nonrigid free-form registration using landmark-based statistical deformation models. In: *Proc. SPIE 8314, Medical Imaging 2012*. p. 8314:42.
- Rueckert, D., Frangi, A., Schnabel, J., 2001. Automatic construction of 3d statistical deformation models using non-rigid registration. In: *MICCAI 2001, LNCS 2208*. pp. 77–84.
- Rueckert, D., Sonoda, L., Hayes, C., Hill, D., Leach, M., Hawkes, D., 1999. Nonrigid registration using free-form deformations: application to breast mr images. *IEEE Trans Med Imaging* 18 (8), 721–721.
- Sadowsky, O., Chintalapani, G., Taylor, R., 2007. Deformable 2d3d registration of the pelvis with a limited field of view, using shape statistics. In: *In Proc. of MICCAI 2007, LNCS 4792*. p. 519526.
- Sariali, E., Mauprivez, R., Khiami, H., Pascal-Mousselard, H., Catonne, Y., 2012. Accuracy of the preoperative planning for cementless total hip arthroplasty. a randomised comparison between three-dimensional computerised planning and conventional templating. *Orthop Traumatol Surg Res* 98, 151158.
- Schumann, S., Sato, Y., Nakanishi, Y., Yokota, F., Takao, M., Sugano, N., Zheng, G., 2015. Cup implant planning based on 2-d/3-d radiographic pelvis reconstruction-first clinical results. *IEEE Trans Biomed Eng* 62 (11), 2665–2673.

- Shen, D., Davatzikos, C., 2002. Hammer: hierarchical attribute matching mechanism for elastic registration. *IEEE Trans Med Imaging* 21 (11), 1421–1439.
- Sodickson, A., Baeyens, P., Andriole, K., Prevedello, L., Nawfel, R., Hanson, R., Khorasani, R., 2009. Recurrent ct, cumulative radiation exposure, and associated radiation-induced cancer risks from ct of adults. *Radiology* 251 (1), 175–184.
- Tristan, A., Arribas, I., 2007. A fast b-spline pseudo-inversion algorithm for consistent image registration. In: *CAIP 2007, LNCS 4473*. pp. 768–775.
- Vercauteren, T., De Gersem, W., Olteanu, L.A.M., Madani, I., Duprez, F., Berwouts, D., Speleers, B., De Neve, W., 2013. Deformation field validation and inversion applied to adaptive radiation therapy. *Phys. Med. Biol.* 58 (15), 5269–5286.
- Vercauteren, T., Pennec, X., Perchant, A., Ayache, N., 2009. Diffeomorphic demons: efficient non-parametric image registration. *Neuroimage* 45 (Suppl. 1), S61–S72.
- Whitmarsh, T., Humbert, L., De Craene, M., Del Rio Barquero, L., Frangi, A., 2011. Reconstructing the 3d shape and bone mineral density distribution of the proximal femur from dual-energy x-ray absorptiometry. *IEEE Trans Med Imaging* 30 (12), 2101–2114.
- Yao, J., Taylor, R., 2003. Assessing accuracy factors in deformable 2d/3d medical image registration using a statistical pelvis model. In: *In Proc. of ICCV 2003*. pp. 1329–1334.
- Yan, C., Zhong, H., Murphy, M., Weiss, E., Siebers, J.V., 2010. A pseudoinverse deformation vector field generator and its applications. *Med Phys* 37 (3), 1117–1128.
- Zheng, G., 2010a. Effective incorporating spatial information in a mutual information based 3d-2d registration of a ct volume to x-ray images. *Comput Med Imag Grap* 34, 553–562.
- Zheng, G., 2010b. Statistically deformable 2d/3d registration for estimating post-operative cup orientation from a single standard ap x-ray radiograph. *Ann Biomed Eng* 38 (9), 2910–2927.

- Zheng, G., 2011. Personalized x-ray reconstruction of the proximal femur via intensity-based non-rigid 2d-3d registration. In: In Proc. of MICCAI 2011, LNCS 6892. pp. 598–606.
- Zheng, G., Gollmer, S., Schumann, S., Dong, X., Feilkas, T., Gonzalez Ballester, M., 2009. A 2d/3d correspondence building method for reconstruction of a patient-specific 3d bone surface model using point distribution models and calibrated x-ray images. *Med Image Anal* 13 (6), 883–899.
- Zheng, G., Yu, W., 2015. Non-rigid free-form 2d-3d registration using statistical deformation model. In: Proc. MLMI 2015, LNCS 9352. pp. 102–109.