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A New Osteophyte Segmentation Algorithm Using the Partial Shape Model and Its Applications to Rabbit Femur Anterior Cruciate Ligament Transection via Micro-CT Imaging

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Abstract

Osteophyte is an additional bony growth on a normal bone surface limiting or stopping motion at a deteriorating joint. Detection and quantification of osteophytes from computed tomography (CT) images is helpful in assessing disease status as well as treatment and surgery planning. However, it is difficult to distinguish between osteophytes and healthy bones using simple thresholding or edge/texture features due to the similarity of their material composition. In this paper, we present a new method primarily based on the active shape model (ASM) to solve this problem and evaluate its application to the anterior cruciate ligament transaction (ACLT) rabbit femur model via micro-CT imaging. The common idea behind most ASM-based segmentation methods is to first build a parametric shape model from a training dataset and then apply the model to find a shape instance in a target image. A common challenge with such approaches is that a diseased bone shape is significantly altered at regions with osteophyte deposition misleading an ASM method and

eventually leading to suboptimum segmentations. This difficulty is overcome using a new partial-ASM method that uses bone shape over healthy regions and extrapolates it over the diseased region according to the underlying shape model. Finally, osteophytes are segmented by subtracting partial-ASM-derived shape from the overall diseased shape. Also, a new semiautomatic method is presented in this paper for efficiently building a 3-D shape model for an anatomic region using manual reference of a few anatomically defined fiducial landmarks that are highly reproducible on individuals. Accuracy of the method has been examined on simulated phantoms while reproducibility and sensitivity have been evaluated on micro-CT images of 2-, 4- and 8-week post-ACLT and sham-treated rabbit femurs. Experimental results have shown that the method is highly accurate ($R^2 = 0.99$), reproducible ($ICC = 0.97$), and sensitive in detecting disease progression (p values: 0.065, 0.001, and <0.001 for 2 weeks versus 4 weeks, 4 weeks versus 8 weeks, and 2 weeks versus 8 weeks, respectively).

Keywords

Active shape model (ASM); anterior cruciate ligament transection (ACLT); micro-computed tomography (micro-CT) imaging; osteophyte; rabbit femur; segmentation

I. Introduction

Musculoskeletal disorders are associated with the formation of new bones at two main sites—the joint margin (osteophytosis) and ligament and tendon insertions (enthesophyte formation) [1], [2]. An osteophyte is an additional bony growth on a normal bone surface limiting or stopping motion at a deteriorating joint and often pressurizing nearby nerves causing pain and sometimes debilitating medical conditions. Osteophytes are strongly associated with osteoarthritis (OA), probably developing in response to abnormal stress on the joint margin [3]. There is also evidence in literature that marginal osteophytes may develop as an age-related phenomenon not related to any joint disease [4]. OA is a progressive joint disease characterized by cartilage degradation and bone remodeling. OA affects nearly 27 million people in the U.S. and problems with ambulation secondary to OA may account for 25% of visits to primary care physicians, so the burden to society is quite high [5]. It is estimated that 80% of the population will have radiographic evidence of OA by the age of 65, although only 60% of those will show symptoms [5]. Several research reports exist in the literature studying the size and the pattern of osteophyte distributions in patients with symptoms of OA in different joints [6]–[9].

Besides pain and other OA related symptoms, osteophytes may also lead to development of other diseases including dysphagia [10] and pneumonia [11]. However, osteophytes may not always lead to clinical symptoms and some are formed as a part of the normal aging process [4]. Also, osteophytes may not require treatment unless they are causing pain or damaging other tissues. Recently, there has been research interest in studying the role of retained osteophytes in causing pain and other symptoms in patients with total knee or hip arthroplasty [12], [13]. An effective tool to detect and derive a quantitative measure of osteophyte morphology in patients will be helpful in clinical and research studies and in understanding the cause and etiology of related disease progression. Such a tool may prove

useful for diagnostic purposes and for planning and monitoring surgical and therapeutic interventions. Radiographs provide an insensitive and inaccurate way of detecting the shape and position of osteophytes [14], [15]. Recently, MRI and computed tomography (CT) imaging modalities, which provide 3-D information, have been adopted for osteophyte detection and quantification [6], [16]–[18]. However, these methods rely on visual detection and scoring of osteophytes in 3-D images. In this paper, we present a new method for osteophyte segmentation and quantification. We evaluate its performance using simulated phantoms as well as micro-CT images of distal femurs from an anterior cruciate ligament transection (ACLT) rabbit model [18], [19].

Image segmentation is a process of identifying and delineating the spatial extent of a target object in an image. There are several established approaches for image segmentation, and extended surveys on medical image segmentation methods exist in the literature [20]. Despite a large number of segmentation approaches available in the literature, it has remained an active research area due to unique requirements by individual segmentation tasks. In this paper, we design a method for segmenting osteophytes in micro-CT images which may also be useful to segment and quantify osteophytes in patients via CT imaging. Development of such methods is important as it is difficult to distinguish between osteophytes and healthy bones using simple thresholding or edge/texture features due to the similarity of their material composition. We, therefore, present a new method primarily based on the active shape model (ASM) to solve this problem and evaluate its application to the ACLT rabbit femur model via micro-CT imaging. The premise of our method is to, first, determine the healthy bone in the image scan data and then subtract it leading to segmentation of osteophytes. This two-step approach facilitates reducing segmentation errors induced by wide variations in shape, smoothness, and size of osteophytes.

The common idea behind most ASM-based segmentation methods [21] is to first build a parametric shape model from a training dataset and then apply the model to locate a shape instance in a given test image. However, such an approach faces an immediate self-imposing challenge due to the fact that bone shape/geometry is maximally distorted at regions affected by osteophyte deposition. Therefore, a straightforward application of a prior-shape model to determine the target shape in a test image is bound to be influenced by the geometry of the osteophyte itself. A possible solution to this problem is to use the shape information from healthy bone surface regions and use that information to extrapolate the original surface at regions affected by osteophytes. This observation has inspired us to formulate a new approach, called the partial ASM (pASM) that uses bone geometry over regions with higher compliance to the prior shape model and uses the so-computed shape parameters to extrapolate bone shape over regions with imperfect match possibly due to osteophyte presence. Another important contribution of this paper is to design a generic approach to build an ASM for a 3-D object using interactive inputs for a few fiducial landmarks (LMs) that are reproducibly locatable in a training dataset. Experimental results evaluating the method's accuracy, reproducibility, and sensitivity based on simulated phantoms and micro-CT images of ACLT rabbit femurs are presented. Theory and algorithms for a new method to build an ASM for any 3-D anatomic body region along with the pASM are presented in Section II. Methods and the experimental setup for the specific application of segmenting

osteophytes in ACLT rabbit femur via micro-CT imaging are described in Section III. Finally, all experimental results are discussed and conclusions are drawn in Section IV.

II. Theory and Algorithms

An osteophyte or bone spur [see Fig. 1(a)] is an additional bony growth on a normal bone surface [see Fig. 1(b)] which is often difficult to separate from the healthy bone using simple thresholding in CT/micro-CT imaging as demonstrated in Fig. 1(c). As illustrated in Fig. 1(d), a straightforward application of a shape-model-based approach, e.g., the ASM, fails to segment the healthy bone in the presence of osteophytes due to the influence of diseased regions. As mentioned earlier, this difficulty is overcome by using a new approach of the pASM introduced in this paper. Theoretical and methodological developments related to 3-D shape model generation are described in Section II-A while those related to the pASM are presented in Section II-B.

A. New Approach to 3-D Active Shape Modeling

Major challenges in developing a shape model for a given anatomic structure lie in defining the anatomic shape as an ordered set of LMs on each individual shape instance in a training dataset. Although the task is less challenging in two dimensions (2-D), it is not the case in 3-D. Several research works have been reported in the literature on 3-D LM generation toward developing a shape model [22]–[31]. Kelemen *et al.* [22] solved the 3-D point correspondence problem through a shape parameterization technique by using spherical harmonics. Davies *et al.* [29] introduced a new approach that poses the LM correspondence task as an optimization problem on the quality of the statistical model that minimizes the description length of the resulting model. This approach has further been studied and improved by Thodberg [30] and Heimann *et al.* [31]. Registration-based approaches have been adopted by several research groups [23]–[28] to develop the correspondence of 3-D LMs within a set of training shapes. Brett and Taylor [23] developed a framework for automatic 3-D LM generation via a binary tree of registered and merged pairs of shapes, each represented by a set of polygonal contours which was further modified in [24]. Wang *et al.* [25] used a surface-registration method based on a metric matching surface-to-surface distance, surface normal, and curvature to establish the correspondence of 3-D LMs. Frangi *et al.* [26]–[28] have used a volumetric free-form elastic registration technique based on the maximization of normalized mutual information to build the 3-D LM correspondence within the set of training shapes.

Here, we develop a new method for defining the shape model of a given 3-D anatomic surface inspired by the approach we intuitively follow in 2-D. For example, while defining the shape model of a hand, we indicate a few salient points (solid dots in Fig. 2) and then automatically include a predefined number of equispaced additional points (hollow dots in Fig. 2) in between every two successive salient points. On a 3-D anatomic surface, often, several curves and LM points may anatomically be defined and manually detected with high reproducibility; we refer to these LMs as *fiducial LMs*. The idea is to interactively indicate such curves and LM points on a given shape using a graphical interface and use these curves and LM points as reference to divide the entire 3-D surface into subsurface

regions. Using the reference of interactive fiducial LMs, additional LMs are automatically located on each subregion according to a predefined distribution; we refer to such LMs as *secondary* LMs. We argue that such an approach is more reproducible and efficient leading toward an optimal tradeoff between automatic and manual landmarking. The presented approach of 3-D LM generation is fundamentally different from other registration-based methods [23]–[28]. Here, a complex anatomic 3-D surface is divided into smaller subregions and piecewise geodesic deformations are used to accomplish the LM correspondence over the entire surface. This approach provides a synergistic coupling between manual input and computerized automatic techniques. This objective is fulfilled using several new algorithms. The new 3-D shape model generation method consists of six sequential steps: 1) define the fiducial LM system; 2) indicate fiducial LMs on individual training shapes; 3) define complete LM set on one prototype training shape; 4) generate LM mesh on the prototype shape; 5) warp the complete set of prototype LMs on each individual training shape using the correspondence of fiducial LMs; and 6) compute the shape model. In the following, we describe each of these steps in more detail.

1) Fiducial LM System—The purpose of fiducial LM system is to divide the anatomic shape surface into subsurfaces and indicate a few anatomic LM points that are reproducible. An example of a fiducial LM system on a rabbit femur is illustrated in Fig. 3; anatomic references of fiducial LMs are described in Section III-A2. Two types of fiducial LMs are used here: 1) LM curves and 2) LM points as illustrated in Fig. 3. Let $C_1, C_2, \dots, C_{N_C}$ denote the fiducial LM curves and let $P_1, P_2, \dots, P_{N_P}$ denote the fiducial LM points. It may be noted that all fiducial LM points $P_1, P_2, \dots, P_{N_P}$ are the members of the complete LM set. The fiducial LM curves are designed to partition the entire femur bone surface region into subregions, say, $R_1, R_2, \dots, R_{N_R}$ where each subregion R_i is bounded by a circular sequence of LM curves $C_{i1}, C_{i2}, \dots, C_{in}$. It may be noted that a subregion R_i may contain one or more fiducial LM points $P_{j1}, P_{j2}, \dots, P_{jm}$; however, there may be subregions containing no LM point.

2) Fiducial LMs on Individual Training Shape—The fiducial LM curves and points are manually drawn on a training shape through a graphical interface described in Section III-A3. A fiducial LM curve is drawn using a sequence of control points on a shape surface and eventually represented as a B-spline projected on the anatomic surface; again, the method to derive such a B-spline is presented in Section III-A3. A LM curve C_i is essentially a mapping function $f_i: [0, 1] \rightarrow \mathbb{R}^3$, where $\mathbb{R}$ is the set of real numbers. A LM curve may be altered by moving, deleting, or adding its control points. Finally, a fiducial LM point P_j is a point on the anatomic surface of a given training shape.

3) Complete LM Set on a Prototype Training Shape—One of the training data is used as a prototype shape and the complete set of LMs, denoted by Ω , is defined on the prototype shape with reference to its fiducial LMs. As discussed earlier, the complete LM set should contain both fiducial as well as secondary LMs. Following the shape model theory [21], Ω must be an ordered set of a predefined number of LM points. To comply with this requirement, a set of a predefined number of equispaced LMs are automatically identified on each LM curve. Now onward, a fiducial LM point or an automatically

identified LM point on a fiducial LM curve will be referred to as a *primary LM*. Furthermore, for each anatomic subregion R_i on the prototype shape, an extended list of secondary LMs is interactively specified through a graphical interface at an approximate uniform distribution. Let Π denote the set of all primary LMs and let Θ denote the set of all secondary LMs; thus, the complete LM set $\Omega = \Pi \cup \Theta$. We will use Π_i and Θ_i to denote the set of primary and secondary LMs on the subregion R_i . In general, we will use p and s to refer to a primary and a secondary LM, respectively, and l to refer to any LM from Ω .

4) LM Mesh Generation—The LM mesh on a given training shape is generated from its binary representation using the following steps. First, a surface mesh representation of a binary object [see Fig. 4(a)] is computed using the marching cube algorithm [32]. This surface mesh is highly dense [see Fig. 4(b)] yielding around 15–20 thousand triangles and consists of the finest elements in our computational framework determining the intrinsic precision of the method. The LM mesh that is much coarser in resolution is generated using the following steps: 1) augmentation of surface-mesh ensuring that each LM in Ω is a vertex of the surface mesh; 2) computation of manifold distance transform; and 3) manifold Delaunay triangulation and LM mesh generation.

Augmentation of surface mesh: The primary objective of this step is to ensure that each LM is a vertex of the final surface mesh. A mesh is represented by a pair $Y = (V, E)$, where V is the set of all vertices and E is the set of all edges in Y . The marching cube algorithm ensures that the vertices and the edges in Y partition the entire surface into triangular elements while maintaining the topology of the surface. However, a primary or a secondary LM is not necessarily a vertex of the surface mesh which is computed independently. In case an LM is not a vertex of the surface mesh, it may either be located inside a surface-mesh triangle or on its edge. When an LM l falls inside a triangle abc , where a , b , and c are the surface-mesh vertices, the triangle abc is replaced by three smaller triangles, namely, abl , lbc , and alc and therefore the original mesh $Y = (V, E)$ is augmented to $Y_{\text{aug}} = (V \cup \{l\}, E \cup \{\overline{al}, \overline{bl}, \overline{cl}\})$. On the other hand, if l falls on an edge $\overline{ab}$, the triangle abc is replaced by two triangles alc and $b lc$ and the mesh is modified to $Y_{\text{aug}} = (V \cup \{l\}, (E - \{\overline{ab}\}) \cup \{\overline{al}, \overline{bl}, \overline{cl}\})$. These mesh augmentation steps are illustrated in Fig. 4(c). In the subsequent discussion, a surface mesh Y will refer to the augmented surface mesh with every LM being a vertex of the mesh.

Computation of manifold distance transform: The intuitive idea behind this step is to generate a geodesic Voronoi neighborhood diagram of the LMs embedded on a surface mesh. Computation of planar Voronoi neighborhood diagram [33] is accomplished using regular Euclidean distance metric. On the other hand, a manifold distance metric is necessary to compute manifold Voronoi neighborhood diagram which is described in the following.

A *path* π on a surface mesh $Y = (V, E)$ between two vertices $v_1, v_2 \in V$ is a sequence of edges $\langle e_1, e_2, \dots, e_n \rangle \forall i, e_i \in E$ that satisfies the following three conditions.

1. v_1 is a vertex of e_1 .

2. v_2 is a vertex of e_n .
3. e_i and e_{i+1} share a common vertex.

The length of a path $\pi = \langle e_1, e_2, \dots, e_n \rangle$, denoted by $\mathcal{L}(\pi)$, is defined as $\mathcal{L}(\pi) = \sum_{i=1}^n |e_i|$, where $|e_i|$ denotes the Euclidean length of the edge e_i . There are infinitely many paths on a surface mesh between any two vertices; let $\mathcal{P}(v_1, v_2, Y)$ denote the set of all paths on a surface mesh Y between two vertices v_1 and v_2 . Finally, the manifold distance $\mathcal{D}(v_1, v_2, Y)$ between v_1 and v_2 on Y is defined as follows:

$$\mathcal{D}(v_1, v_2, Y) = \min_{\pi \in \mathcal{P}(v_1, v_2, Y)} \mathcal{L}(\pi).$$

In order to compute the manifold Voronoi neighborhood diagram, we need to determine manifold distance transform from LMs along with the information about the nearest LM. This objective is fulfilled using the following algorithm, where $\mathcal{N}_Y(v)$ denotes the neighborhood of v in the mesh Y that is defined as the set of all vertices in Y sharing an edge with v :

```

begin: compute_manifold_distance_transform

: surface-mesh  $Y = (V, E)$ 

      set  $\Omega$  of all LMs

output: manifold distance transform map  $\text{MDT} : V \rightarrow \mathbb{R}$ 

      nearest LM map  $\text{NLM} : V \rightarrow \Omega$ 

      initialize an empty queue  $Q$ 

for all  $v \in V$ 
     $\text{MDT}(v) = \text{MaxValue}$ 
     $\text{NLM}(v) = -1$ 

for all  $I \in \Omega$ 
     $\text{MDT}(I) = 0$ 
     $\text{NLM}(I) = I$ 
    push  $I$  in  $Q$ 

while  $Q$  is not empty
  pop  $v$  from  $Q$ 
  for all  $v' \in \mathcal{N}_Y(v)$ 
    if  $\text{MDT}(v') > \text{MDT}(v) + |vv'|$ 
       $\text{MDT}(v') = \text{MDT}(v) + |vv'|$ 
       $\text{NLM}(v') = \text{NLM}(v)$ 

```


push v' in Q

end compute_manifold_distance_transform

A result of the aforementioned algorithm is presented in Fig. 4(d) and (e) illustrating both manifold distance transform and manifold Voronoi neighborhood, which is essentially depicting the nearest LM map.

LM mesh generation: LM mesh is generated using the results of the manifold distance transform described in the previous section. Specifically, the LM mesh is created as the manifold Delaunay triangulation of the surface mesh derived using the manifold distance transform and the nearest LM map as follows:

begin: generate_LM_mesh

input: surface-mesh $Y = (V, E)$

set of all LMs Ω

nearest LM map $NLM : V \rightarrow \Omega$

output: LM-mesh $\Psi = (\Omega, E_\Omega)$

initialize an LM-mesh $\Psi = (\Omega, E_\Omega = \text{empty set})$

all $v \in V$

$I_1 = NLM(v)$

for all $v' \in N_Y(v)$

$I_2 = NLM(v')$

if $I_1 \neq I_2$ and $\overline{l_1 l_2} \notin E_\Omega$

$E_\Omega = E_\Omega \cup \overline{l_1 l_2}$

end generate_LM_mesh

To illustrate how the method works, the LM mesh, or, equivalently, the manifold Delaunay triangulation is simultaneously shown in Fig. 4(e) with color-coded manifold Voronoi neighborhoods of LMs.

Here, an interesting question may transpire as whether the aforementioned LM generation method creates unnecessary edges in a mesh destabilizing its topology. Topological stability may be examined at each individual vertex in the LM mesh $\Psi = (\Omega, E_\Omega)$ as follows. A vertex $v \in \Omega$ is a *stable vertex* if its neighboring vertices $v_0, v_1, \dots, v_{n-1} \in \Omega$ form a unique cyclical order of the edges $\overline{v_0 v_1}, \overline{v_1 v_2}, \dots, \overline{v_{n-2} v_{n-1}}, \overline{v_{n-1} v_0} \in E_\Omega$ creating a simple closed loop and $\overline{v_i v_j} \notin E_\Omega$ for all $j \neq i \pm 1 \pmod n$. As examined using a computerized algorithm, the aforementioned algorithm has always generated a stable surface mesh for the datasets used in our experiment. It may be noted that, even if the method fails to generate a topologically stable mesh in an adverse situation, the instance may automatically be detected and unnecessary edges may be deleted.

Deformation of reference LMs onto another bone surface: The basic idea of this step is to map secondary LMs of a reference surface onto a target surface using the correspondence of their primary LMs. This task is accomplished using piecewise deformation of each subregion of the reference surface onto the corresponding subregion of the target surface, where the correspondence of two subregions is defined by their primary LMs. Let R denote a subregion on the reference surface containing the primary LMs $p_1, p_2, \dots, p_n$ and secondary LMs $s_1, s_2, \dots, s_m$ and let R' denote the matching subregion on the target surface containing primary LMs $p'_1, p'_2, \dots, p'_n$. Note that, at this stage of computation, no information is available about secondary LMs on the target surface. The problem here is to deform the secondary LMs $s_1, s_2, \dots, s_m$ onto the target subregion R' such that 1) the correspondence of primary LMs in two surfaces is preserved, i.e., p_i is mapped onto p'_i for all $i = 1, 2, \dots, n$ and 2) the geometry of the LM mesh in R is minimally changed after mapping secondary LMs of R onto R' . A method similar to a physical process of spring-mesh deformation is adopted here as follows. Let $E_R \subset E_\Omega$ denote the set of the edges such that one endpoint of the edge is a secondary LM inside R and the other end is any LM of R ; thus, E_R along with the LMs of R describe the LM mesh over the subregion R . Note that E_R excludes all edges between two primary LMs on R . A spring mesh with uniform spring constant is constructed by replacing each edge of E_R with a spring of length equal to that of the edge itself [green edges in Fig. 5(b)]. A manifold spring deformation process is adopted that starts with the best possible alignment between p_i s (red dots) and p'_i s (yellow dots). Subsequently, each p_i gradually moved toward p'_i using an external force and the secondary LMs are allowed to freely move along the surface of R' governed by the spring force system while preserving the mesh topology. Each primary LM moves in straight line joining its initial and final positions. However, to ensure that the final destination of a secondary LM lies on the geodesic of R' , its movements is always constricted along the geodesic of the target surface. To complete the description of the process, the force system and the mesh topology preserving conditions are defined in the following paragraph.

The LM mesh deformation process is defined as an iterative process and the duration of each iteration is a predefined constant ∇t . At any time/iteration t during the deformation process, two different types of forces are used—one for primary LMs and the other for secondary LMs. As mentioned before, the mesh deformation process is initialized by aligning primary LMs $p_1, p_2, \dots, p_n$ of R with the LMs $p'_1, p'_2, \dots, p'_n$ of R' , respectively, using the affine transform τ computed by Procrustes analysis [34] [see Fig. 5(b)]. Thus, $p_i(t=0) = \tau(p)$ denotes initial position of a primary LM p_i in the process of deforming the reference LM mesh of R onto the target subregion R' . Similarly, $s_j(t=0) = \tau(s_j)$ denotes initial position of a secondary LM s_j during the deformation process. At any time t during the deformation process, a force $\mathbf{F}_p(p_i, t)$ on a primary LM $p_i(t)$ is designed to gradually move p_i toward p'_i and is defined as a constant force along the vector $p'_i - p_i(t)$. The oscillation around the target point p'_i is avoided by forcing $p_i(t)$ to move to p'_i at the end of iteration when they become sufficiently close; it avoids oscillation by stopping over movements. The force $\mathbf{F}_s(s_j, t)$ on a secondary LM s_j is designed to serve two purposes: 1) to enforce the deformation along the geodesic of the target surface R' and 2) to simulate a spring mesh deformation. The first

component of the force is much larger compared to the second component. During the early part of the deformation process, the first component of the force serves the purpose of projecting s_i onto the target surface mesh $Y' = (V', E')$. At any time t during the deformation process, the magnitude of this force on s_i is proportional to the distance of $s_i(t)$ from Y' and is directed toward the closest surface-mesh vertex $v \in V'$; let us use $\mathbf{F}_{DT}(x, Y')$ to denote the force on any point $x \in \mathbb{R}^3$ that pulls x toward the surface Y' . At any time t during the deformation process, the spring force $\mathbf{F}_{sp}(s_i, s_j, t)$ on an LM s_i due to the edge $\overline{s_i s_j}$ is governed by the following equation:

$$\mathbf{F}_{sp}(s_i, s_j, t) = K \times \frac{(l_{\text{orig}}(s_i, s_j) - |s_i(t) - s_j(t)|)}{l_{\text{orig}}(s_i, s_j)} \times \frac{(s_i(t) - s_j(t))}{|s_i(t) - s_j(t)|}$$

where K is the spring constant and the function $l_{\text{orig}}(s_i, s_j)$ gives the original length of the edge connecting the two LMs s_i and s_j after the affine transformation τ , i.e., $l_{\text{orig}}(s_i, s_j) = |\tau(s_i) - \tau(s_j)|$. Finally, the total force $\mathbf{F}_s(s_i, t)$ on a secondary LM s_i at time t is defined as follows:

$$\mathbf{F}_s(s_i, t) = \mathbf{F}_{DT}(s_i(t), Y') + \sum_{l \in N_Y(s_i)} \mathbf{F}_{\text{spring}}(s_i, l, t)$$

where $N_Y(s_i)$ denotes the neighborhood of s_i in the LM mesh. Two additional constraints are imposed on the deformation of secondary LMs to preserve a mesh topology and to avoid mesh folding on the target surface as described in the following. Let u denote the new position of an LM s_i after applying the force $\mathbf{F}_s(s_i, t)$, as defined earlier, over a duration of ∇t . This move is allowed, i.e., $s_i(t + \nabla t)$ is updated to u , if it preserves the mesh topology and creates no folding through the narrow space between the target surface and the deforming LM mesh itself (see Fig. 6). This phenomenon of folding, mostly associated with a geodesic mesh deformation, seems to be a new observation and may easily be confused with mesh topology violation. Such a phenomenon occurs when the springs attached to a specific vertex [e.g., vertex a in Fig. 6(a)] gets highly compressed. Due to finite step size of iterations during the deformation process, under high compression, the vertex a may flip on the other side of the most convenient edge [the edge $\overline{bc}$, Fig. 6(a)] and glides through the narrow space between the triangle abc and the bone surface beneath the mesh [see Fig. 6(b)]. Essentially, the vertex a creates a folding at the edge bc to produce some extra geodesic space releasing the high compression exerted on itself. A solution to this problem is to never allow an LM to come close to another LM or an edge of the LM mesh or an LM triangle. On the other hand, a mesh topology is altered under one of the following three conditions: 1) an LM coincides with another LM; 2) an LM transects an edge of the LM mesh; and 3) an LM transects through a mesh triangle. The final result of an LM mesh generated using the topology preserving the elastic mesh deformation algorithm is presented in Fig. 5(c).

B. Partial Active Shape Model

A shape of an anatomic structure is mathematically represented using the mean shape as well as shape variations observed in the set of training shapes leading to an ASM [21]. Following the outline by Cootes and Taylor [21], the mean as well as variations in an anatomic shape is computed using the Procrustes method [35] and principal component analysis (PCA). Specifically, in 3-D, the mean shape is represented as a $3N$ -D vector μ and the shape model is expressed by the following equation:

$$\alpha = \mu + Pb$$

where 1) N is the number of LMs in Ω ; 2) α is a shape instance derived from the shape model; and 3) $P = (p_1, p_2, \dots, p_k)$ is a matrix of k eigenvectors corresponding to k largest eigenvalues computed using the PCA of training shapes; and b is a k -D shape-control vector. It may be noted that, essentially, μ represents mean positions of the LMs in Ω ; let Ω_0 denote these positions. Similarly, for any given shape-control vector b , the resulting α represents an instance of the LMs, say Ω_b .

The ASM has been widely applied in medical image segmentation [28], [36]–[40]. The common idea behind all ASM-based segmentation methods is to find a shape instance governed by the underlying ASM that optimally fits to the shape intuitively defined in a target image. A major disadvantage of such an approach, especially in the context of medical imaging, is that the anatomic shape is significantly altered around diseased regions and the ASM is misguided by the altered shape of diseased regions which no longer complies the normal distribution of healthy shapes and it leads to artifacts in segmentation results. Here, we propose a new pASM method that uses image-feature-defined partial shape over healthy regions to control ASM parameters while discarding its misguidance over diseased regions. Thus, the pASM essentially interpolates the original shape over diseased regions from the information acquired over healthy regions using the underlying ASM. In the following, we describe the pASM algorithm.

Unlike the approach presented in [21], we directly optimize different parameters under a predefined cost function to segment a target shape in a given image. Specifically, the shape-control vector b and the affine transformation matrix τ are determined that minimize the predefined cost function. First, we want to distinguish the differences between a “shape instance” and a “shape expression”. A shape instance Ω_b is a member of the ASM family and, therefore, is defined by a k -D shape-control vector b . It may be noted that during the generation of the ASM all training shapes are aligned under affine transformation eliminating affine variations among training shapes. Therefore, a shape expression, an occurrence of a shape in an image, needs to be associated with an affine transformation τ embedding a shape instance Ω_b in the image. Thus, a shape expression $\Omega_{\tau b}$ is defined by τ and b , where each LM is derived by applying the affine transformation τ on the corresponding LM of the shape instance Ω_b . Final shape expression is achieved by finding the parameters τ and b that minimize a cost function.

Two types of cost fields, namely, image driven and user driven are used in our segmentation algorithm. Image-driven cost is directly computed from a cost field, where a cost measure is assigned to every point. Specifically, an image-driven cost field is a function $C_{\text{image}} : \mathbb{R}^3 \rightarrow \mathbb{R}^+$, returning a value at each image point, where $\mathbb{R}^+$ denotes the set of positive real numbers including zero. It may be noted that although, C_{image} gives a value at each point in 3-D space, for computational purpose, the cost function is determined only at discrete points and its value at any other point in the 3-D space is computed using bilinear interpolation.

Let $\Omega_{\tau, \mathbf{b}}$ denote the set of NLMS constituting a shape expression. The idea of the pASM is to estimate the image-driven cost for a shape expression from M NLMS in $\Omega_{\tau, \mathbf{b}}$ with smaller cost values. Specifically, the image-driven cost $\varphi_{\text{image}}(\tau, \mathbf{b})$ for $\Omega_{\tau, \mathbf{b}}$ is defined as follows:

$$\varphi_{\text{image}}(\tau, \mathbf{b}) = \sum_{p \in \Omega'} C_{\text{image}}(p)$$

where $\Omega' \subset \Omega_{\tau, \mathbf{b}}$ is the set of NLMS with M smallest image-driven costs. It is expected that in a diseased region, the shape deviation is large and, therefore, is filtered out in cost estimation of a shape expression.

The user-driven cost $\varphi_{\text{user}}(\tau, \mathbf{b})$ for $\Omega_{\tau, \mathbf{b}}$ is determined from a finite set S_{user} of user-defined reference points as follows:

$$\varphi_{\text{user}}(\tau, \mathbf{b}) = \sum_{p \in S_{\text{user}}} \min_{q \in \Omega_{\tau, \mathbf{b}}} |p - q|.$$

Finally, the cost $\varphi(\tau, \mathbf{b})$ is defined as the sum of image-driven and user-driven costs, i.e.,

$$\varphi(\tau, \mathbf{b}) = \varphi_{\text{image}}(\tau, \mathbf{b}) + \varphi_{\text{user}}(\tau, \mathbf{b}).$$

Once the cost function is determined, the pASM algorithm may be formulated as follows:

begin: compute_pASM

input: a pre-computed ASM: $\alpha = \mu + P\mathbf{b}$

image-driven cost field $C_{\text{image}} : \mathbb{R}^3 \rightarrow \mathbb{R}^+$

user defined reference points S_{user}

a user defined affine transformation τ_0 for initial shape expression number of points M for computing image-driven cost

output: optimized shape expression $\Omega_{\tau, \mathbf{b}}$

initialize shape expression $(\tau_0, \mathbf{b}_0 = [0, 0, \dots, 0]^T)$

assign $(\tau_{\text{cur}}, \mathbf{b}_{\text{cur}}) = (\tau_0, \mathbf{b}_0)$

```

do
    assign ( $\tau_{pre}, b_{pre}$ )=( $\tau_{cur}, b_{cur}$ )
     $\tau_{cur} = \arg \min_{\tau} \phi(\tau, b_{pre})$ 
     $b_{cur} = \arg \min_b \phi(\tau_{cur}, b)$ 
while  $\Omega_{\tau_{cur}, b_{cur}}$  does not converge
end compute_pASM

```

In the current implementation of the aforementioned algorithm, the affine transformation τ_0 for the initial shape expression is determined by the user via a GUI described in the next section. Optimizations steps for τ_{cur} and b_{cur} are implemented using the Powell conjugate gradient descent method [41], [42]. The convergence criterion for this algorithm is defined using movements of all LMs. Specifically, the average movement of an LM over the last $2m$ iterations, where m is a predefined number, is used to define stabilization of an LM. Finally, the algorithm terminates when all LMs stabilize, i.e., the largest among average movements of all LMs is smaller than a threshold ε_{av} . This condition for convergence succeeds in terminating the process even when there is an oscillation at one or more LMs. Finally, the location of an LM is determined as its mean position over the last $2m$ iterations

III. Experimental Methods

In this section, we describe methods and experimental designs related to the specific application for osteophyte segmentation in ACLT rabbit femurs via micro-CT imaging. The two distinct steps in our osteophyte segmentation algorithm are 1) ASM generation for rabbit femurs from a training dataset and 2) osteophyte segmentation on individual test data using the rabbit femur ASM. Application-specific details for these two steps are presented in Section III-A and -B, respectively, while experimental plans and methods to evaluate the osteophyte segmentation algorithm are described in Section III-C.

A. Training and ASM Generation

The method for generating a rabbit femur ASM, described in this section, is essentially based on the algorithm presented in Section II-A. Here, we explain the details of the training phase adopted for the current application. Specifically, we describe the following steps: 1) animal preparation and image acquisition of ACLT rabbit femurs and preprocessing; 2) LM systems for rabbit femurs defined by a clinician, and 3) GUI for specifying LMs on each individual training data and the final ASM.

1) Animal Preparation, Image Acquisition, and Preprocessing—All animals were prepared according to the following procedures approved by the Merck Institutional Animal Care and Use Committee (IACUC) and micro-CT images were acquired from excised distal femurs of ACLT rabbits 2, 4, and 8 weeks following surgery ($N = 6, 6, \text{ and } 8$, respectively) [43]. Another group of nine animals underwent sham surgeries and were used as controls. All images were acquired and reconstructed at isotropic $32.5 \mu\text{m}$ resolution using a Scanco micro-CT-40 CT imaging instrument. Each micro-CT image from the training set was preprocessed to comply with requirements for subsequent steps. First, the bone region was

segmented from each micro-CT image using a simple thresholding algorithm [44], [45], second, the largest component was identified [46], and, third, noisy voxels forming tiny islands were eliminated. Finally, the marrow space in each femur bone was filled using a morphological closing operation [47].

2) Rabbit Femur LM System—Leporidae femoral bony anatomy, quite similar with a few exceptions to its human structural analog, provides several definite features which readily allow for the construction of a fiducial landmarking system. These features, including global anatomical regions such as the long axis of the femoral medullary canal as well as femoral medial/lateral condyles, specific sulci and fossae, articulation features, and specific tendon insertion sites, allow for the creation of highly repeatable anatomical landmarking system of points, curves, and subregions (see Fig. 3). Using the user interface described in the following section, the creation of the fiducial LMs begins by identifying basic geometric regions using anatomic global references. Initially, the entire surface is subsectioned with the use of reference planes, creating first a center (sagittal) plane through the femur by bisecting the condylar articulating surfaces through the patellar ridge. A second sectioning plane, orthogonal to the long axis of the femur, demarcates the upper bounds of the surface using the anterior margin of the patellar ridge as a repeatable reference. Following the generation of these sections, additional regions are identified and curves created by tracing along the margins of 1) femoral condyles; 2) lateral and medial patellar ridges; 3) sesamoid articulation fossae; and 4) popliteal sulcus. Additional reference LMs (points) are created by identifying insertion sites for the sesamoid ligaments, sesamoid articulation surfaces, and the origin of the long extensor muscle. This system of landmarking was found to provide a highly repeatable fiducial system for the entire CT training set.

3) Landmarking and ASM Generation—Once a fiducial LM system for rabbit femurs is defined, the next major step is to identify these LMs on each training image data. For this purpose, we have designed and developed a new GUI system allowing to interactively locate LMs on an anatomic structure. Most available GUI systems provide functions to manipulate points, lines, and curves on a 2-D plane. The new GUI system, called a geodesic editor, is designed to allow a user to directly interact on a geodesic surface facilitating LM definitions on a given anatomic structure. In the following paragraphs, we describe the methodology toward realizing the essential features of a geodesic editor.

Geodesic points: A user should be able to interactively deploy, select, move, and delete any LM point on a geodesic surface. This step may be accomplished using a 2-D to 3-D surface backprojection algorithm.

Geodesic straight line: A user should be able to draw a geodesic straight line, projection of a Euclidean straight line on a geodesic surface, by indicating two points on an anatomic surface. A geodesic straight line may be computed in following steps: 1) find the straight line in 3-D space joining the two indicated points and 2) project each point of the straight line onto the closest point on the surface. Each individual end points of the geodesic straight line may be selected and freely moved on the surface.

Geodesic curve: This feature should allow a user to draw a geodesic curve by placing a sequence of control points on a surface and, subsequently, altering the curve as needed. A geodesic curve is computed by iteratively performing the following three steps until a convergence is reached: 1) compute a B-spline in 3-D space using the sequence of control points; 2) project the B-spline onto the target surface yielding a geodesic curve; and 3) generate a new sequence of control points by sampling the newly computed curve at a uniform interval. Although the convergence of the method has not been theoretically proven, it successfully converged within five iterations for several hundred geodesic curves tested in our laboratory. Once a curve is drawn on a surface, a user should be able to select a control point on the curve and freely move it along the surface or even delete the point. Also, the user should be allowed to add new control points anywhere on the curve. Furthermore, the curve may be divided into two parts by selecting a point on it.

Reference plane: Reference planes are often useful in defining LMs on an anatomic structure. An effective GUI design should allow the provision of generating a reference plane in 3-D space, freely moving, rotating, and deleting it. A user should also have an option to select the geodesic curve at the intersection between the plane and the target surface as a new LM edge. In this experiment, micro-CT images of femur bones from nine sham treated rabbits and six 2-week ACLT animals with visually limited osteophytes were used in the training phase for developing femur shape model. Altogether 37 fiducial LM curves and 4 LM points were manually identified on the femur surface of each training dataset using the custom-built GUI described earlier. From these fiducial LMs, a total of 216 primary LMs and 307 secondary LMs were automatically computed on each of the training femur shape, which were then used for ASM generation.

B. Osteophyte Segmentation

As mentioned earlier, an osteophyte is a bony growth protruding over a healthy cortical bone surface [see Fig. 1(a)]. The basic approach of segmenting osteophytes as adopted here is to determine the healthy bone surface using the statistical shape model computed from healthy animals by the training step discussed in Section III-A. To improve the segmentation results, a new pASM method, described in Section II-B, is adopted here. It uses bone geometry of regions with good fit and extrapolates the shape over diseased region(s) using the statistical shape model. The overall flow chart of our osteophyte segmentation method is presented in Fig. 8 and in the following, we describe each of these modules.

1) Preprocessing and Cost Field Computation—The purpose of the preprocessing step is to generate a solid region including both bone and osteophyte voxels from the acquired micro-CT image of each test specimen. This task is accomplished using the steps used during training as stated in Section III-A1 and an output of this step is illustrated on the second column in Fig. 9. In Section II-B, we mentioned an image-derived cost field C_{image} which is a driving factor of the pASM algorithm. Here, we discuss the computation of the cost field C_{image} from the preprocessed image. Let $O \subset \mathbb{Z}^3|_{\mathcal{Z}}$ is the set of integers denote the set of voxels inside the solid region obtained after preprocessing. A two-sided binary distance transform $DT_O: \mathcal{Z} \rightarrow \mathbb{R}^+$ is computed as follows:

$$DT_o(p) = \begin{cases} \min_{q \in O} |p-q|, & \text{if } p \in O \\ \min_{q \in O} |p-q|, & \text{if } p \in \bar{O} \end{cases} \quad \text{where } \bar{O} = \mathcal{X}^3 - O.$$

The image-derived cost field C_{image} is computed using the two-sided distance transform as follows:

$$C_{\text{image}}(p) = DT_o(p) \quad \text{for all } p \in \mathcal{X}^3.$$

Finally, at any 3-D point in the Euclidean space, the image cost value is computed using bilinear interpolation of the cost values at eight closest voxels. Although the method presented in Section II-B allows user-specified reference points, no such points were used in our current experiment.

2) pASM Algorithm and Osteophyte Segmentation—A detailed algorithm for the pASM method has been presented in Section II-B. The algorithm requires an initialization of the affine transformation τ_0 and the shape parameter b_0 to define the initial shape expression. For the shape parameter, we use the zero vector $[0, 0, \dots, 0]^T$, i.e., the mean shape itself. On the other hand, a manual initialization through a graphical interface is used to select the initial affine transformation τ_0 . Here, we have used the Powell's algorithm for optimizing both affine transformation as well as shape parameters. Osteophyte segmentation was obtained by subtracting the shape expression determined by the pASM from the combined region constituting of healthy bone and osteophytes and then applying a morphological opening. Specifically, regions with thickness value of half a voxel or less in the difference image are considered as effects of segmentation error or subject-specific geometric variations and are excluded from osteophyte regions. Results of osteophyte segmentation for different rabbit femur data are visually illustrated in Fig. 9. For quantitative analyses, we computed total osteophyte volume (in mm^3) and average osteophyte heights (in mm). Osteophytes volume and average height were computed in units of mm^3 and mm, respectively, using the knowledge of image resolution.

C. Experimental Plans and Methods

Experiments were designed to examine the accuracy of the method on simulated data and to evaluate the reproducibility and sensitivity of the method using the micro-CT data of ACLT rabbit femurs described in Section III-A1. In the following sections, we describe these experiments in detail.

1) Accuracy Analysis—Due to difficulties with generating the truth for osteophytes in real images, we have designed the accuracy evaluation experiment on simulated data. A manual outlining of osteophytes in 3-D images is extremely tedious and may suffer from subjectivity errors. Therefore, we have developed an algorithm to simulate osteophytes on healthy bone surfaces that allows interactive specifications of affected regions and also the severity of osteophytes. The simulation process starts with a manually outlined region on a

healthy bone surface [see Fig. 10(a)] and completes osteophyte deposition in three steps [see Fig. 10(b)]: 1) generate a flat top hill (red); 2) add small hills (green) on the flat top; and 3) add a random white noise (black). For each simulated data, the ground truth for osteophyte volume and height was computed by subtracting the healthy bone from the simulated bone with osteophytes. The linear correlation between a true measure of simulated osteophyte and the corresponding measure of computed osteophyte was studied.

2) Reproducibility Analysis—The reproducibility experiment was designed on osteophyte segmentations of 2-, 4-, and 8-week ACLT data of rabbit femurs performed by three independent users. The osteophyte segmentation method requires user input for initialization of the mean shape of the ASM with respect to a given femur shape. Specifically, initial rotation, translation, and scale to the mean shape are manually indicated by a user using a graphical interface and the rest of the segmentation process is completed automatically. Three users independently initialized the mean shape. Volume and height measures for osteophytes were derived from each segmentation result and intraclass correlation in terms of interclass correlation value (ICC) value of each osteophyte measure for the three users was computed.

3) Sensitivity Analysis—The experiment for sensitivity analysis of the method was designed using the three groups of micro-CT images from 2-, 4-, and 8-week ACLT rabbit femurs. Specifically, the sensitivity of the method was evaluated by examining the method's ability to separate each of the three groups using the volume/height measures from segmented osteophytes. An unpaired t-test was performed for a given osteophyte measure between each two groups to measure the sensitivity of the specific measure. The analysis was carried out based on the measures from segmentation results by the first user as well as on the mean result from the three users.

IV. Results

Results of rabbit femur shape model are presented in Fig. 7(c). Although 523 LMs were used to denote a femur shape, a compact rabbit femur shape model representation was accomplished using only seven eigenvectors corresponding to seven largest eigenvalues covering 86% of total shape variation in our training dataset. More complete coverage of shape variations may be achieved by including more eigenvectors. However, considering the limited number of samples in the training dataset, we have chosen to restrict the shape model to the subspace defined by the seven eigenvectors corresponding to the largest seven eigenvalues. Variations of computed femur shapes due to shifts along each of the three eigenvectors corresponding to the three largest eigenvalues are presented in Fig. 7(c). As it visually appears, computed shapes successfully capture the basic shape of a rabbit femur except that the surface appears smoother as caused by PCA-based data reduction.

Results of osteophyte segmentation on micro-CT images of ACLT rabbit femur are qualitatively illustrated in Fig. 9. The first row illustrates the results of the entire process on a 2-D image slice. Segmentation results for osteophyte using the pASM algorithm are presented in the last two columns. Overall, the segmentation results of osteophytes are visually satisfactory. Narrow differences between the original healthy bone and segmented

bone are mostly caused by relative rigidity in a shape model and wide subject-specific variations in femur shapes. However, osteophytes caused by such thin layers of mismatches are easily eliminated by morphological filtering operations described in Section III-B2. The last three rows in the same figure present computerized osteophyte segmentation on 2-, 4-, and 8-week ACLT rabbit femurs via micro-CT imaging. As it appears visually, the 2-week ACLT femur exhibits only a small region with osteophyte while the 4- and 8-week ACLT femurs have grown significant osteophytes. Although it is difficult to quantitatively measure the accuracy of the obtained segmentations, the results are visually satisfactory. The pASM algorithm was implemented on a desktop PC with In-tel Xenon 2.0 GHz CPU running under Linux OS. The algorithm has converged in 50–200 iteration taking ~10 s on an average.

The accuracy of the method is examined on simulated osteophyte phantom data described in Section III-C1. Specifically, we have selected micro-CT data of two 2-week and two 4-week sham-treated rabbits and used those as normal shapes for generating simulated osteophytes. Altogether, 16 simulated osteophyte samples were generated with different amounts of osteophytes at different locations. Three samples with small, medium, and large simulated osteophytes on one healthy femur data [see Fig. 11(a)] are illustrated in Fig. 11. For each simulated osteophyte dataset, the figure displays osteophyte bone phantom and computerized segmentation of osteophytes. To facilitate the visual perception of osteophyte segmentation results, we have adopted a 3-D color rendition scheme, where the color at a surface location indicates the local height of segmented osteophytes. For each osteophyte phantom, the scale indicating the relationship between color and osteophyte height in millimeter unit is given. In these color renditions, surface regions in dark blue indicate healthy bone surface while those in red correspond to regions with maximum osteophyte heights. While the results in Fig. 11 provide a qualitative sense of goodness of the segmentation method, the results of quantitative analyses are presented in Fig. 12. Specifically, the linear correlation between true and computed osteophyte measures was studied and the results are presented graphically. As shown in Fig. 12, both computed osteophyte volumes and average heights show strong linear correlation ($R^2 = 0.99$) with corresponding true measures. Moreover, the best-fit lines for both cases pass through the vicinity of origin with a slope close to 1 indicating the similarity between true and computed measures. The normalized mean absolute error of computed osteophyte volume as compared with the true volume was 6%. The normalized mean absolute error of average osteophyte height was 7%. These results show that computed osteophyte measures are highly correlated with the true measures.

As described in Section III-C2, the reproducibility of the segmentation method was examined by comparing segmentation results from three independent experts. Osteophyte segmentation results obtained with shape model initializations by three independent users on micro-CT images of 20 ACLT rabbit femurs (2-week: 6, 4-week: 6, and 8-week: 8) are presented in Fig. 13. Average percent error (error = ratio of standard deviation and mean of repeat measures) for osteophyte volume was 5.37% while that for osteophyte height was 5.77%. ICC values for both osteophyte volume and height were 0.97 indicating a high reproducibility of osteophyte measures from three independent users. Sensitivity of the osteophyte segmentation method was determined by analyzing the ability of an osteophyte measure to separate each of the 2-, 4-, and 8-week groups; see Fig. 14 for osteophyte

measures for different groups. As described in Section III-C3, for each of the two computed osteophyte measures, we conducted unpaired t-test for measures from every pair of groups and the results are presented in Table I. For the longer effect groups, namely, G4-8: 4-week versus 8-week and G2-8: 2-week versus 8-week, the null hypothesis was rejected with high confidence (p value <0.002) even for the limited number of specimens used for our experiment. For the early-effect group G2-4: 2-week versus 4-week, the results marginally failed to be statistically significant (volume: p value = 0.063, height: p values = 0.065). Relatively weaker sensitivity of osteophyte measures for the early effect group G2-4 may be caused by a compounding effect of multiple factors including the limited number of animals and the variability in response time to ACLT among animals. We expect that the sensitivity for this group will increase if a larger numbers of animals are used.

V. Conclusion

In this paper, a new semiautomatic method has been presented for building a 3-D shape model for a given anatomic site. The uniqueness of the method is that it distinguishes fiducial LMs from ordinary LMs, where the former type of LMs are assigned with a prior anatomic reference and may interactively be detected on an object with high confidence. Also, the fiducial LMs are fewer in number and may either be a point or geodesic curves. The ordinary LMs, which are relatively much larger in number as compared to fiducial LMs, are automatically generated with the reference of fiducial LMs. Unlike the 2-D case, the generation of ordinary LMs from the reference of fiducial LMs is not straightforward and the problem is solved using several new techniques including geodesic Voronoi neighborhood computation, geodesic LM mesh generation from a set of LMs on a surface, deformation of a reference mesh onto any surface using an elastic mesh deformation and correspondence of a fewer fiducial LMs. The method presents a practical solution for 3-D shape model generation with enhanced efficiency and robustness. A new pASM has been introduced to extrapolate healthy anatomic shape over the diseased region. Applications of the two methods to segment osteophytes have been studied in this paper. Accuracy of the method has been evaluated on simulated phantom data while reproducibility and sensitivity of the method have been examined on micro-CT data of ACLT rabbit femur bones. Experimental results have demonstrated high accuracy and reproducibility of the method. Despite that only a limited number of specimens were used in our experiments, the method could distinguish between 2-week versus 8-week and 4-week versus 8-week ACLT rabbit groups with high statistical confidence; the separation between 2-week and 4-week ACLT rabbit groups was marginally less than statistically reliable. It may be noted that the number of specimens was limited in this study. As the sample size increases, the segmentation results will be further refined. Currently, we are studying the application of the method to clinical CT images of OA patients. This approach faces additional challenges triggered by 1) lower resolution of clinical CT imaging and 2) possible wide variation of bone shapes in healthy people. It may be mentioned that it is also difficult to distinguish between osteophytes and healthy bones radiographically [14], [15].

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Fig. 1.

(a) and (b) 3-D renditions of rabbit femur bones with and without osteophytes. (c) 2-D display of osteophytes in a micro-CT image; no visible intensity difference exists between osteophytes and healthy bones. (d) Example of osteophyte segmentation by a conventional ASM approach.

Fig. 2.
Salient (solid dots) and derived (hollow dots) LMs on a 2-D contour of a hand.

Fig. 3. Illustration of fiducial LM curves (red), points (blue), and subregions defined on a femur rabbit bone surface using anatomical guidance.

Fig. 4.

(a) 3-D rendition of a binarized rabbit femur bone data used as a training shape. (b) Surface-mesh representation of (a). A zoom-in representation of the surface mesh is presented on the left to illustrate the mesh structure and triangle density. (c) Graphical illustration of the mesh augmentation process; see the text for details. (d) Manifold distance transform from LM points; the color bar is given on the right. (e) Color-coded display of nearest geodesic neighbor; here each LM is represented by a unique color.

Fig. 5.

Results of reference LM mesh deformation onto a target surface. (a) Initial superimposition of reference mesh (red: LM, green: edge) with the target surface. Results on one subregion: (b) affine alignment of primary LMs using Procrustes analysis and (c) topology preserving elastic deformation of reference LM mesh onto the target surface. *Reference*: red (primary LM), blue (secondary LM), and green (spring-edge). *Target*: yellow (primary LM).

Fig. 6.

Schematic illustration of LM mesh folding through the narrow space between the target surface and deforming LM mesh. Mesh configuration before (a) and after (b) folding. The triangle abc flips on the other side of the edge $\overline{bc}$ and slides through the narrow space between the mesh surface (shown by black lines) and the underlying target surface. Different shadings are used to denote layerwise depths with black lines being front most. Such situation creates a topological aberration of the surface mesh by “folding”.

Fig. 7.

Intermediate steps in computation of a rabbit femur ASM. (a) Manually identified primary LM curves (red lines) and points (blue dots) on a training rabbit femur surface reconstructed from micro-CT data after preprocessing and marrow filling. For comparison see clinical references in Fig. 3. (b) Complete set of primary (red and blue dots) and secondary (green dots) LMs. (c) Shape instances computed from the rabbit femur ASM.

Fig. 8.
Overall work flow chart for osteophyte segmentation.

Fig. 9.

First row Illustration of results at different intermediate steps in the osteophyte segmentation. *From left to right*: Sagittal image slice from micro-CT image of an ACLT rabbit femur, filled-in region for bone with osteophytes, image-derived cost field, segmented healthy bone region, and osteophytes. Although the results on this row are shown in 2-D, all processes were performed in 3-D. *Last three rows from left to right*: Results of osteophyte segmentation on 2-, 4- and 8-week ACLT rabbit femur data. Each row presents two matching views of original bone and osteophyte segmentation. Osteophyte segmentation results are illustrated using a color coding scheme on osteophyte height given at the last column. Here, healthy bones are displayed in dark blue.

Fig. 10.

Illustration of osteophyte simulation. (a) Manually outlined region for osteophyte simulation. (b) Description of the three steps of osteophyte simulation along the line shown in (a). See the text for further clarification.

Fig. 11.

Illustration of simulated osteophytes and the segmentation results. Three rows display examples with small, median, and large simulated osteophytes on femur of a control animal. *From left to right in the first row:* original bone, simulated osteophytes, results of osteophyte segmentation, and the color coding scheme. Here, at any point, color indicates the height of the segmented osteophyte at the corresponding location. Thus, surface regions in dark blue represent the healthy bone. *From left to right in last two rows:* simulated osteophytes, two views of osteophyte segmentation results, and the color coding scheme.

Fig. 12. Results of accuracy analysis on simulated osteophyte phantoms. (a) Linear correlation between true and computed osteophyte volumes. (b) Same as (a) but for average osteophyte heights.

Fig. 13.

Results of reproducibility analysis of osteophyte segmentation in micro-CT images of ACLT rabbit femurs. (a) Interclass correlation of osteophytes volumes using shape model initialization by three independent users. (b) Same as (a) but for average osteophyte heights.

Fig. 14.

Results of sensitivity analysis of osteophyte segmentation in micro-CT images of ACLT rabbit femurs. (a) Computed osteophyte volumes for 2-, 4-, and 8-week ACLT rabbit femurs. (b) Same as (a) but for average osteophyte heights.

TABLE I

Results of Sensitivity Analysis

Osteophyte measures		2-week	4-week	8-week	2-week vs. 4-week	4-week vs. 8-week	2-week vs. 8-week
Volume (mm^3)	mean:	116.9	mean: 169.0	mean: 289.5	p-value:	p-value:	p-value
	std:	34.7	std: 44.7	std: 65.2	0.063	0.002	<0.001
Average height(μm)	mean:	77.0	mean: 110.2	mean: 206.0	p-value:	p-value:	p-value:
	std:	24.4	std: 26.9	std: 47.4	0.065	0.001	<0.001

Results of sensitivity analysis for two osteophyte measures to separate 2-, 4-, and 8-week ACLT rabbit femurs via μ CT. Columns 2–4 present mean and standard deviation values of different measures for individual groups while Columns 5–7 present the p-value of unpaired t-test for each pair of groups.