Computer Methods and Programs in Biomedicine 67 (2002) 85–103

Computer Methods and Programs in Biomedicine

www.elsevier.com/locate/cmpb

Recent development on computer aided tissue engineering — a review

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Received 1 July 2000; accepted 30 October 2000

Abstract

The utilization of computer-aided technologies in tissue engineering has evolved in the development of a new field of computer-aided tissue engineering (CATE). This article reviews recent development and application of enabling computer technology, imaging technology, computer-aided design and computer-aided manufacturing (CAD and CAM), and rapid prototyping (RP) technology in tissue engineering, particularly, in computer-aided tissue anatomical modeling, three-dimensional (3-D) anatomy visualization and 3-D reconstruction, CAD-based anatomical modeling, computer-aided tissue classification, computer-aided tissue implantation and prototype modeling assisted surgical planning and reconstruction.

Keywords: Computer-aided tissue engineering; Tissue engineering; Anatomic modeling; Medical modeling

1. Introduction

Tissue engineering, the science and engineering of creating functional tissues and organs for transplantation, integrates a variety of scientific disciplines to produce physiologic 'replacement parts' for the development of viable substitutes, which restore, maintain or improve the function of human tissues [1–8]. The principles of tissue engineering is that tissues can be isolated from a patient, expanded in tissue culture and seeded into a scaffold prepared from a specific building material to form a scaffold guided three-dimensional (3-D) tissue [9]. The construct can then be grafted into the same patient to function as a replacement tissue. Blood vessels attach themselves to the new tissue, the scaffold dissolves, and the newly grown tissue eventually blends in with its surroundings. The technology developed in the tissue engineering has been used to create various tissue analogs including skin, cartilage, bone, liver, nerve, and vessels [10–20].

The success of tissue regeneration lies heavily on the structural formability of the tissue scaffold and its bioreactor with the seeding cells. The structural scaffolds are formed from structural elements such as pores, fibers or membranes, which can be ordered according to stochastic, fractal or periodic principles and can also be manufactured reproducibly using engineering ap-

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0169-2607/02/$ - see front matter
PII: S0169-2607(01)00116-X

proaches [21–23]. When a 3-D tissue structure is used to develop artificial tissue substitutes, one can even engineer structural design of the biomaterial in the scaffolding architecture to optimize structural and nutritional conditions. Towards this effort, many advances in tissue engineering have been made in biomaterial science, biomechanics, optimization of tissue integration and function in vivo, and design, syntheses, and fabrication of advanced tissue scaffold. Today's computer-aided technologies, medical imaging, modern design and manufacturing have further assisted in those advances and created new possibilities in the development of tissue engineering. Such possibilities include, for example, using non-invasive computed tomography (CT) or magnetic resonance imaging (MRI) techniques to generate tissue structural views for 3-D anatomical model, for tissue classification and trauma/tumor identification [24–33], using computer-aided design/computer-aided manufacturing (CAD/CAM) and rapid prototyping (RP) technology to fabricate the physical models of hard tissues, tissue scaffolds, and the custom-made tissue implant prostheses [34–42], and applying the anatomical and physical modeling for reconstructive surgeons and tissue implementation [43–47].

The utilization of computer-aided technologies in tissue engineering has evolved in the development of a new emerging field of computer-aided tissue engineering (CATE). Driven by the computer imaging technology, CAD/CAM and modern design and manufacturing technology, we classify the field of CATE into following three major categorizes, (1) computer-aided tissue anatomical modeling; (2) computer-aided tissue classification; and (3) computer-aided tissue implantation. The overall view of CATE is described in Fig. 1.

The objective of this article is intent to review some of the salient advances in the field of CATE, with emphasizing on the recent development and application of enabling computer-aided technology, imaging technology, design and manufacturing technology in tissue engineering. The presentation of this article is organized as follows. Section 2 describes computer-aided tissue anatomical modeling, 3-D anatomy visualization and 3-D reconstruction. Section 3 introduces computer-aided tissue classification. Section 4 reports the prototype modeling assisted tissue implantation and surgical planning. Section 5 presents the summary and the conclusion.

2. Computer-aided anatomic modeling and 3-D reconstruction

Anatomical modeling is being undertaken in two primary areas, (1) the development of artificial replacements for tissues where the characterization of natural tissue behavior is needful so as to be able to specify realistically the artificial replacement or synthetic stimulant; and (2) tissue modeling related to the diagnostic area through using artificial materials, mathematical approach, and continuum formulations [48,49]. As human body is not an engineering or mathematically definable object, therefore, anatomical modeling is usually generated through non-invasive imaging technique, such as CT or MRI technology.

2.1. CT/MRI defined anatomical tissue representation

CT produces closely spaced axial slices of patient anatomy that, when rejoined in the appropriate manner, fully describe a volume of tissue. In CT imaging, a 3-D image of an X-ray absorbing object is reconstructed from a series of two-dimensional (2-D) cross-sectional images. An X-ray beam penetrates the object, and transmitted beam intensity is measured by an array of detectors. Each such 'projection' is obtained at a slightly different angle as the scanner rotates about the object. Each CT slice image is computed of tiny picture elements (pixels). Each pixel, in turn, is actually a small volume element (voxel) of patient tissue sampled by the CT scanner [43]. Of the existing methods for generating an anatomical model of a physical part, only CT can non-destructively dimension internal as well as external surfaces [50–52]. However, CT scanning that is used only to create a mirror image model of any organ could not be ethically justified, because of the dose of radiation administered (approximately

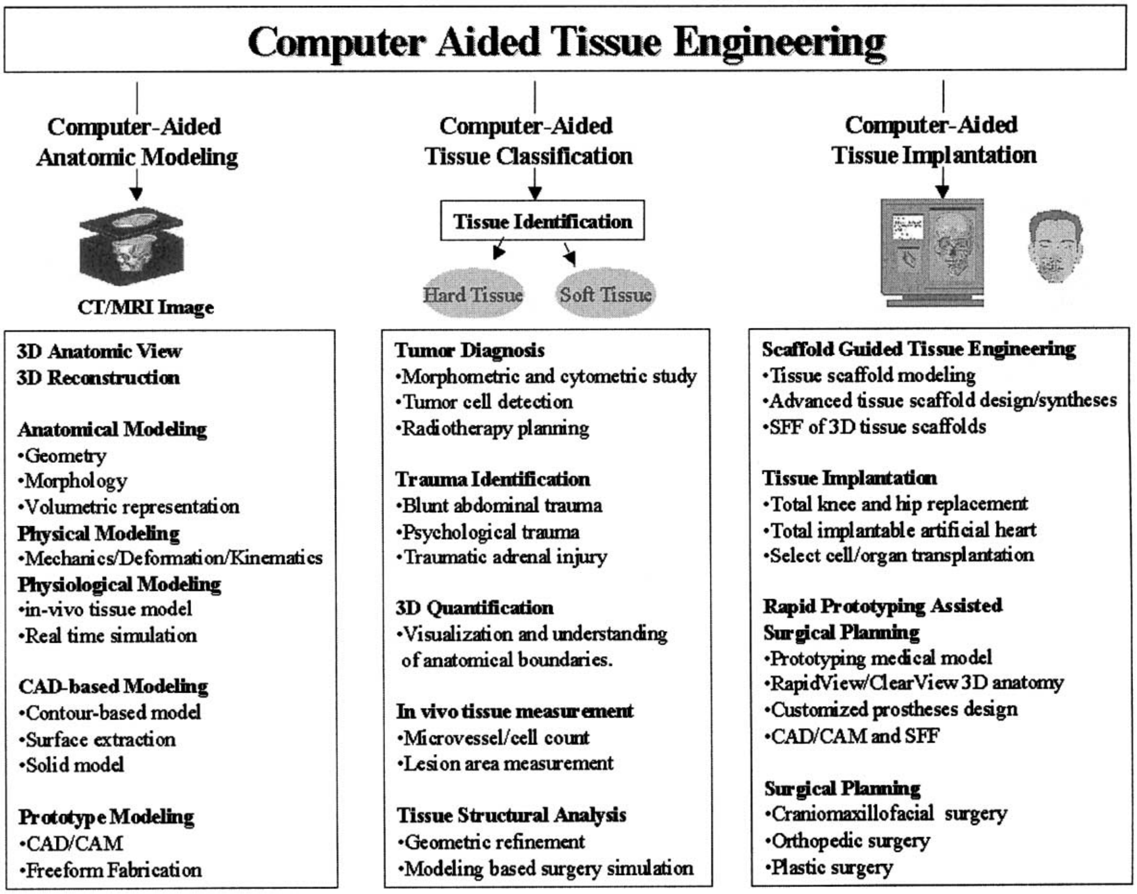

Fig. 1. Overview of computer aided tissue engineering.

30-40 mGy). The advent of MRI has become increasingly popular for its ability to show subtle differences in soft tissue anatomy without the harmful effects of ionizing radiation present in CT. MRI scanning is a non-invasive alternative that projects a 3-D image of the soft tissues together with bone. MRI has proved invaluable in visualizing pathology in soft tissue, especially in neurologic, musculoskeletal, and vascular diseases [43]. Disadvantage of using MRI is the length of time that a patient is required to be exposed and remain motionless during scanning.

Table 1 summarizes a comparison of the basic imaging characteristics commonly used in producing 3-D reconstruction CT and MRI [43].

Table 1
Characteristics comparison of CT and MRI

Characteristics	CT	MRI
Matrix size (pixels)	512×512	256×256
Voxel size (mm)	$0.5\times0.5\times2.0$	$0.5\times0.5\times1.5$ (gap)
Density resolution	4096 levels (12 bit)	128 levels (16 bit)
Signal-to-noise ratio	High	Moderate
Segmentation	Threshold	Complex
Protocol	Simple (radiation)	Complex (benign)

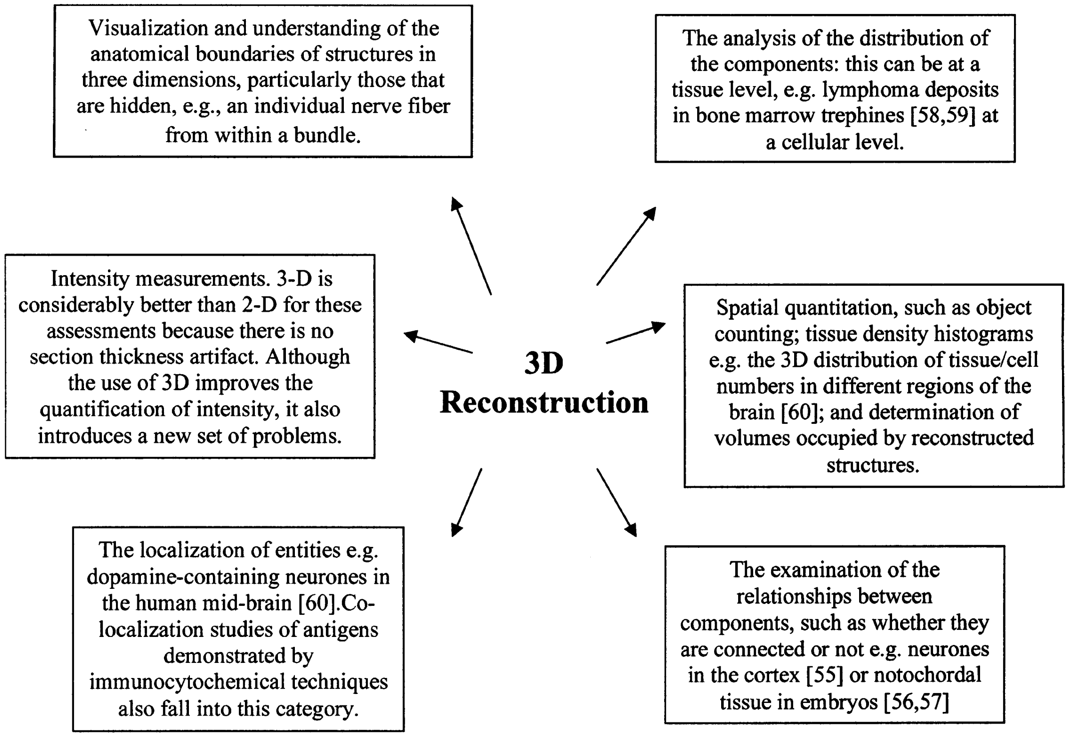

Fig. 2. Three-dimensional reconstruction applications in pathological tissue [61].

2.2. 3-D reconstruction

The loss of the third dimension is an inherent problem with examining sectioned material when the tissue to be examined possesses a complex morphology [53,54]. Techniques in three-dimensional reconstruction (3-DR) allow the third dimension to be studied directly by the displaying of 3-D anatomical images or models. Reconstructed images or models can be viewed in any orientation as contour stacks with hidden lines removed; as wire-frame models; or as shaded, solid models with variable lighting, transparency, and reflectivity. Volumes and surface areas of the reconstructed objects may be determined. Three-dimensional reconstruction of a volumetric data set is usually accomplished by extracting a region of interest (ROI), bounding surfaces to make a closed structure, defining the edges, and reconstructing the surface from ROI to ROI throughout the image set. Fig. 2 presents some biological problems that may use the information obtained from 3-DR.

The process of the reconstruction of 3-D anatomic model from CT data is described in Fig. 3. In the roadmap shown in this figure, the CT/MRI images are integrated using 2-D segmentation and 3-D region growth and this volumetric image data extracts more meaningful, derivative images via 3-D anatomic view. The 3-D anatomic view produces novel views of patient anatomy while retaining the image voxel intensities that can be used for volume rendering, volumetric representation and 3-D image representation. These 3-D images lead to the generation of anatomic modeling. Anatomic modeling is used for contour based generation and 3-D shaded surface representation of the CAD based medical models. The shaded surface display of 3-D objects can involve widespread processing of images to create computer representations of objects. Several visualization issues that cannot be resolved by CAD models provide motivation for the construction of prototype model. Prototype modeling is done through additive/constructive processes as opposed to subtractive processes.

Model slicing and model processing lead to model assisted applications like in surgical planning, pre-operative planning, intra-operative planning in computer assisted surgery.

2.3. Three-dimensional image representation

Three-dimensional anatomical image and representation is usually constructed through either segmentation or volumetric representation. Two-dimensional segmentation is extraction of the geometry of the CT scan data set [51–53]. Each slice is processed independently and inner and outer contours of the living tissue are detected, e.g. using a conjugate gradient (CG) algorithm [62,63]. The contours are stacked in 3-D and used as reference to create a solid model usually through skinning operations. Three-dimensional segmentation [64] of the CT data set are able to identify, within the CT data set, voxels bounding the bone and extract a 'tiled surface' from them. A tiled surface is a discrete representation made of connected polygons (usually triangles). The most popular algorithm is the marching cube algorithm [62–67]. In its original formulation, the marching cube method produces tiled surfaces with topological inconsistencies (such as missing triangles) and usually a large number of triangle elements. This method decomposes the complex geometries in 'finite elements' and approximations to the behavior of the system and the quality of approximation depends on the number of these elements and

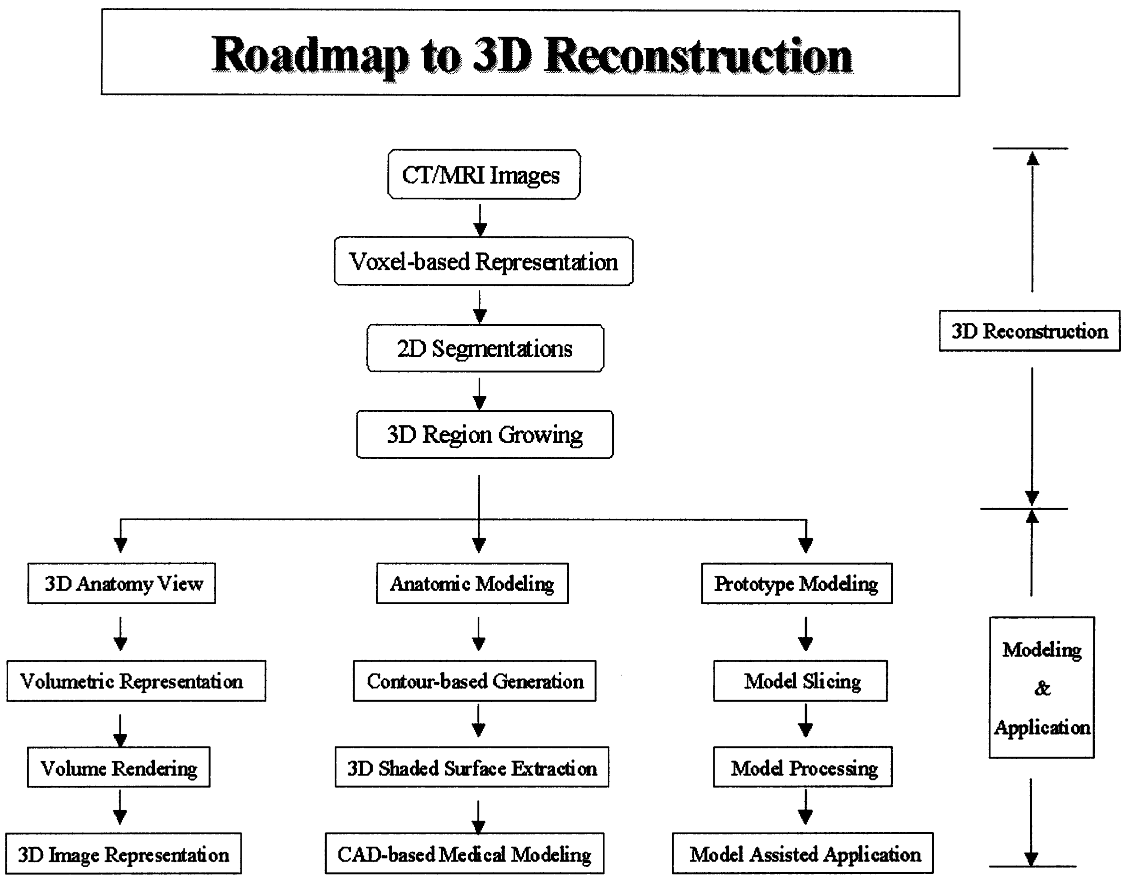

Fig. 3. From CT/MRI to 3-D reconstruction.

the order of the approximation over each element. In the visualization processing, each triangle is treated as separated polygonal entity and the computational requirement scale up exponentially with the number of triangles. To overcome these difficulties, a new algorithm, discretized marching cube (DMC) algorithm is developed for the 3-D segmentation of the CT data set. This algorithm implements various disambiguation strategies which are able to resolve most topological inconsistencies with a reduction of 70% triangle elements and maintaining a high level of geometric accuracy [68].

Volumetric representation encompasses volume rendering leading to the surfaces and their voxel based representation. Three-dimensional volumetric techniques produce the appearance of 3-D surfaces without the computer's having to explicitly define a geometric surface. These 3-D surfaces are computed of tiny picture elements (pixels). Non-dimensional 3-D extensions of pixels are called voxels. A voxel is the basic unit of volumetric representation [69].

Volume rendering [70] deals with the representation of the data to be rendered, along with some of the concepts involved in the handling of this data. Volumetric imaging provides 3-D displays with a continuum of surface and image intensity data [71–80]. The snapshots of the cross sections of these volumetric images are developed as a basis for the computation of the light intensity of the pixels constituting the snapshot. Although, imaging (through CT/MRI) is made in all three planes at the same time, a phase shift in the excitation signal (for all three planes) generates a phase shift in the resulting signal, which allows cross-sectional images to be isolated. Through a clever combination (stacking the cross sections) of image volume projection, gradient intensity mapping, and lighting models, the user-chosen parameters of volumetric imaging can produce 3-D images that range in appearance from conventional projection radiography to shaded-surface displays. These 3-D images not only help in minimizing the errors of interpretation but also provide doctors and surgeons with a 3-D image that could be panned, zoomed and rotated to better locate individual details.

2.4. Anatomic tissue modeling

Beyond the simple reforming of CT scans or MR images into new views [81], 3-D modeling and reconstruction provides a new way of viewing the 3-D anatomy of the patient. These derived imaging's go beyond simple reformatting to provide a view that integrates across slices to produce 'snapshots' of entire organs or bones. A realistic tissue model is desirable for virtual reality surgery training simulators, mechanical tool design and controller design for safe and effective tissue manipulation. The anatomic tissue modeling should result in efficient and realistic estimation of tissue behavior and interaction forces. In general, an anatomic modeling is constructed through either one of the following three approaches.

2.4.1. Contour-based method

Contour-based method generates 3-D-like displays [81–84]. Sliced CT or MRI imaging data produces a series of outline anatomical profiles of interested tissue. This can be achieved by creating a computer-generated contour following a single CT or MR image intensity value, for example, the threshold for cortical bone. The methods of slice-wise collection of tissue borders rely on relatively sophisticated mathematics models designed to take into account large neighborhoods of pixels — often relying on adjacent homogeneity of tissue and defining boundaries at those places where disparate homogeneous areas abut [85–88]. In the process of 3-D reconstruction, the collection of all contours in a slice combine with adjacent slices to form a topographic map — like wireframe of 3-D structure. The wireframe is transformed into a surface by connecting adjacent slice contour segments to form simple polygons (either triangles or quadrilaterals) [89]. The collection of polygons constitute a surface that forms the basis of 3-D display in a process called surface rendering — a type of computer processing of geometric objects that relies on the basis of illumination, reflection, shadowing, and so on, to produce the impression of a 3-D object [90–92].

In general, contour-based processing is computationally simple and can be refined to produce good 3-D displays. However, the transformation from contours to surface is more problematic, often requiring operator guidance in connecting contours from adjacent slices [93]. More sophisticated use of contouring employs methods adapted from computer graphics to blend adjacent contours into a solid surface similar to the popular graphics process called morphing. This shape-based interpolation, when combined with a good lighting model, results in 3-D images that are both detailed and realistic [94].

2.4.2. 3-D shaded surface extraction

More sophisticated methods of 3-D surface extraction use the full 3-D nature of the tomographics data to directly produce a geometric surface description [95–98]. In its simplest form, the data are treated as a true volume of image information. This image volume can be processed by simple threshold following to produce a list of all voxels composing the surface of an object, or a broader, solid-segmentation algorithm might include voxels at or above the specified threshold. Rendering can then proceed by any number of methods, including the rendering of the faces of each voxel [95], the creation of simple polygons from adjacent voxel information [97], or the direct projection of voxels onto a display screen or film [65]. The most detailed surfaces are often constructed by interpolating the surface elements at subvoxel resolution. Surfaces derived from interpolated 3-D thresholding are extremely realistic. The demands of representing the entire surface can require either a large amount of computational power or extreme sophistication in data organization and handling.

Anatomical models constructed through the contour-based and the surface extraction methods only provide surface information. The internal details of the original image will be lost during the surface regeneration. Many 3-D computer systems provide methods to integrate the original CT or MR image data back into the surface representation. This is done by post-processing both the surface rendering and the data volume so that when the surface is cut by user-controlled planes, the appropriate image intensity values are projected back onto the cut surface [99].

2.4.3. CAD-based medical modeling

Although diagnostic devices such as CT/MRI are able to produce accurate 3-D tissue descriptions, however, the voxel-based anatomical representation cannot be effectively used in many biomechanical engineering activities. For example, 3-D surface extraction requires either a large amount of computational power or extreme sophistication in data organization and handing; and 3-D volumetric model, while produce a realistic 3-D anatomical appearance, does not contains geometric topological relation. Although they are capable of describing the anatomical morphology and applicable to RP through a converted STL format, neither of them is capable of performing anatomical structural design, modeling-based anatomical tissue biomechanical analysis and simulation [18–20]. In general, activities in anatomical modeling design, analysis and simulation need to be carried out in a vector-based modeling environment, such as using CAD system and CAD-based solid modeling.

Modern CAD systems use the so-called ‘boundary representation’ (B-REP), in which a solid object is defined by the surfaces which bound it. These surfaces are mathematically described using special polynomial functions such as non-uniform rational B-spline (NURBS) functions. The use of NURBS to develop computer models can be applied and highly recommended in the fabrication of the implant [62–64]. NURBS makes it possible to construct the computer model using fewer numbers of digitized points, which would significantly decrease the size of the files. It also would facilitate operations such as intersection and closure of the boundary surface [100]. Unfortunately, the direct conversion of the CT data set of a human bone into its NURBS solid model is not simple. In the last few years some commercial programs were presented as solutions to this conversion problem, for example, SurgiCAD by Integraph ISS, USA, Med-Link, by Dynamic Computer Resources, USA, and Mimic and MedCAD, by Materialise, Belgium. However, none of these programs has been widely applied in the biomechanical engineering field due to complex, cost, linked to specific clinical application, or not capable enough to generate sophistical model.

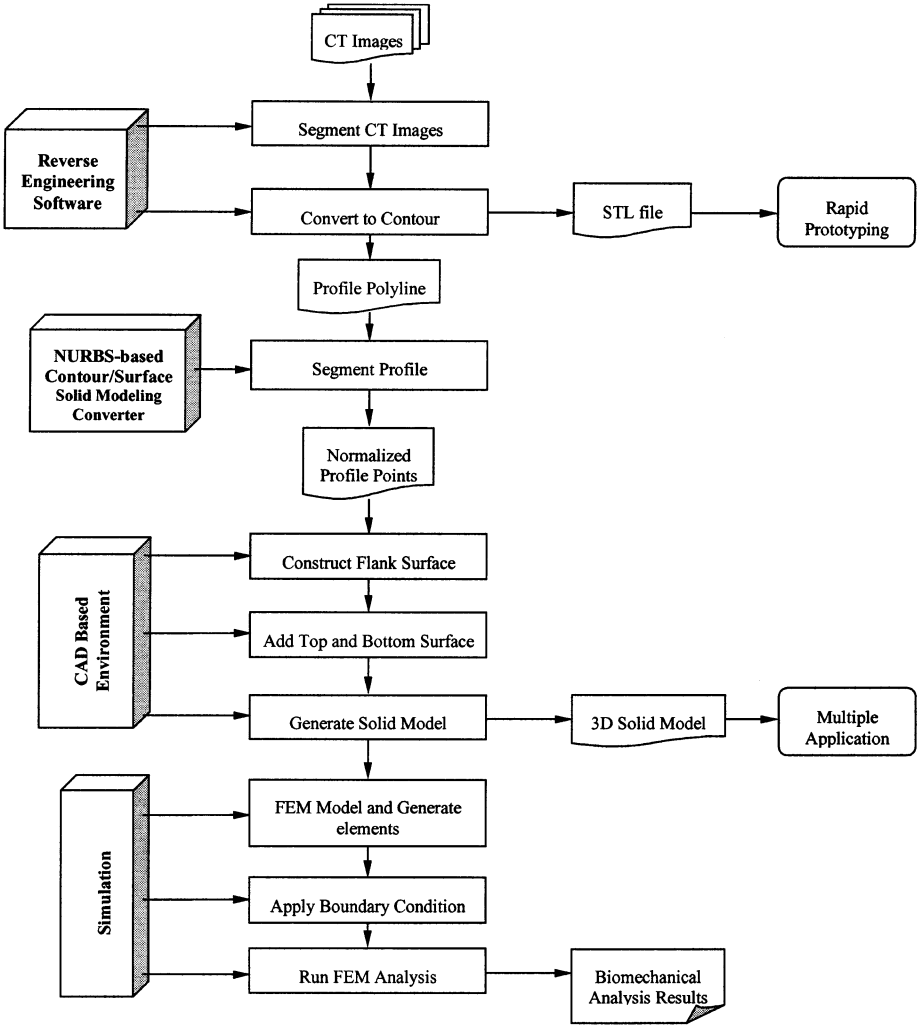

Fig. 4. Framework of developing CAD-based anatomical modeling.

Effective methods for the conversion of CT data into CAD solid models still need to be developed.

A framework of the development and application of CAD-based anatomical modeling is outlined in Fig. 4.

2.5. Rapid prototyping (RP) based medical modeling

Several visualization issues that are addressed but not resolved by virtual computer anatomical models provides the motivation for the construction of physical models of anatomical prototypes,

1. 2-D screen displays do not provide an intuitive representation of 3-D geometry;
2. unusual or deformed bone geometry may be hard to comprehend on-screen;
3. the integration of multiple bone fragments is hard to visualize on-screen;
4. planning complex 3-D manipulations based on 2-D images is difficult.

One of the methods to fabricate physical models of anatomical prototypes and implants is to use CAD/CAM interfaced numerically controlled machine tools. The computer numerical control

(CNC) machines fabricate prototypes by carving away material from the outside of a solid block or sheet of foam, plastic, wax, or metal [101–105]. The limit of this method is the ability to create intricate structures, especially when there is a high degree of internal complexity, for example, to prototype human craniomaxillofacial anatomy.

In the late 1980s, the introduction of RP technologies offered new possibilities for medical modeling [106–109]. RP approach uses the principle of layered manufacturing to create the model layer by layer. This naturally tomography approach lends itself readily to the free-form sculpture present in human anatomy. In RP approach, the CT image is accurately reproduced in a few hours as an physical model which can be handled by the surgeon, allowing an immediate and intuitive understanding of the most complex 3-D geometry used to accurately plan and practice an operative procedure. In addition, RP approach produces extremely detailed models that serve as excellent templates for the creation of custom implants. A physical model manufactured from X-ray CT or MRI data can be held and felt, offering surgeons a direct, intuitive understanding of complex anatomical details, which cannot be obtained from imaging on-screen. A precise physical model can offer an accurate prediction of implant size and type, and provide 'hands-on' surgical planning and rehearsal [110]. Rapid prototyping technology offers the surgeon a tool that is not available anywhere else. This tactile imaging modality provides substantially more information than other 2-D imaging modalities. In addition, rapid prototyping anatomic model can also be used to display local regions of interest, such as surgeon to draw round a tumor on the CT image and have it built into the model for disease diagnosis.

The advantages of adopting anatomical modeling with rapid prototyping for surgery and planning can be summarized as following [37],

1. production of anatomical prototypes from X-ray CT or MRI data for visualization, diagnosis and pre-operative planning;
2. manufacture of artificial limbs from laser or ultrasound data with custom fitting sockets for comfort and long wear;
3. direct production of casting molds for custom surgical implants, CAD designed to match patient data;
4. simulation of surgical procedures;
5. evaluation of prosthesis fit;
6. intra-operative guidance;
7. tangible record for case study.

Steps in the fabrication of a patient model by RP processing [37] are,

1. patient scans with CT/MR imagings;
2. segmentation to delineate and extract the surface as triangles or polygons;
3. model pre-processing to produce a STL file formatted solid model;
4. model slicing by selected RP processing;
5. model fabrication.

Available RP processes commonly used in prototyping anatomical modeling have been summarized in reference [37] as follows.

Stereolithography (SLA), creates models by tracing a lower power ultraviolet laser across a vat filled with resin.

Selective laser sintering (SLS), creates models out of a heat fusible power by tracing a modulated laser beam across a bin covered with the powder.

Fused deposited modeling (FDM), creates models out of heating thermoplastic material, extruded through a nozzle positioned over a computer controlled x–y table.

Laminated object manufacturing (LOM), creates models out of heat-activated, adhesive coated paper, by tracing a focused laser beam to cut a profile on sheets positioned on a computer controlled x–y table.

Multiphase jet solidification (MJS), creates metal or ceramic models out of various low viscosity materials in powder or pellet form, by extruding the build material through a jet in liquid form.

Three-dimensional printing (3-DP), creates models by spraying liquid binder through ink-jet printer nozzles on to a layer of metallic or ceramic precursor powder.

The benefits of physical modeling are independent of the operative/reconstructive method preferred by individual surgeons. The models create a true hands-on replica and portray accurate anatomy and pathology with any operative technique, permitting the selection of most biomechanically sound solution through a realistic pre-operative evaluation and rehearsal. The increased cost of CT scanning and RP should be more than offset by higher success rates, shorter operating times, fewer revisions and, ultimately greater quality of life for patients.

3. Computer aided tissue classification

Tissue classification may be achieved using very simple methods, i.e. thresholding [111] or more complex algorithms (i.e. region growing, [111,112]). For simplex thresholding classification, it is essential that a good contrast of the target and the reference is present. Based on these classification algorithms and thresholding procedures the tissue can be classified into two major categories of hard tissue and soft tissue.

3.1. Classification of hard and soft tissue

Hard tissue mainly encapsulates the bony structures. Since bony structure data transferred into the parametric surface fabrication machine normally show steady properties, the application of spline interpolations is suitable for representing the real contours. Recent development in modeling techniques, computer software and hardware system enables the transfer of bony structures into an acceptable accurate geometric models possible [113]. The key for soft tissue modeling is to model the deformability of soft tissue under the influence of neighboring structures or surgical instruments. Simulation of medical procedures aims at navigation of 3-D anatomical datasets, modeling of physical interaction of each anatomical structure, understanding functional nature of human organs. To achieve these simulations it is essential to model at anatomical, physical and physiological levels. The modeling of soft tissue mechanics and deformation i.e. soft tissue modeling has been identified as a key to achieve the above stated levels. Since the human body is mainly made up of soft tissue, the medical consequence of soft tissue modeling is significant, ranging from neurosurgery, plastic surgery, musculoskeletal surgery, heart surgery, abdominal surgery, minimally-invasive surgery [114–116].

The most challenging task in the field of soft tissue modeling is the simulation of the resulting soft tissue changes during surgery, for which two main approaches can be found.

1. Virtual reality deformable models. Real time simulations of linear elastic properties are based on mechanical models like the mass-spring models [117–123]. Owing to their limitations (like topological design, validity of deformations, dynamic behavior, visualization) of modeling only linear elastic properties, these models are used only to realistically animate tissue deformations, not to simulate the exact physical behavior of human soft tissue [124].
2. Mathematical deformable models. Analytical techniques to mathematically define non-linear, anisotropic and visco-elastic material properties [125–130]. However, these computations are very time consuming and are difficulty in interactively simulating.

Although both the methods are being explored and analyzed, only a few applications have been discovered which provide both real time deformation and physically realistic modeling of complex non-linear tissue deformations. Most of the research in this topic can be found in the field of the deformable modeling in surgical simulation [131].

3.2. Issues on soft tissue modeling

The most valuable 3-D reconstructions are those that represent relationships among both bony and soft tissue anatomy [132–139]. Unfortunately, the routine identification of soft tissue 3-D image volumes remains a significant challenge to medical imaging, although the use of multi-echo MR imaging combined with CT bone data promises to produce excellent integration of tissue albeit in a somewhat computation-intense study. The challenges in this domain are in both soft tissue segmentation and the geometric registration of separate patient imaging studies.

Three main problems for achieving realistic soft tissue models are explained below.

3.2.1. Acquisition of biomechanical information

A major impediment to building accurate soft tissue models is the lack of quantitative biomechanical information suitable for finite element computation. The required information not only refers to the inner mechanical property of a given soft tissue but also includes contact with the surrounding tissues. In terms of computation, the former corresponds to the constitutive law of motion linking the stress tensor with the strain tensor whereas the latter corresponds to the boundary conditions [124]. The acquisition of elastic or viscoelastic properties of a tissue is usually performed by rheological experiments. Existing rheometers require that experiments are performed in vitro on uniaxial samples. This raises two problems. First, the in vitro properties may vary substantially from the true in vivo properties, specifcally with permeable tissues containing incompressible fluids. Second, experiments with uniaxial samples are only valid if the tissue is homogeneous and isotropic. Finally, rheometers do not allow characterization of the force/deformation contact between neighboring tissues.

In the future, medical imaging could provide in vivo biomechanical tissue measurements. Widely used imaging modalities such as CT-scanners or MRI already provide approximate information about the density and the relative water content of tissue. Such information can then be used to infer approximately the biomechanical tissue properties. For instance, Koch et al. [140] derives the stiffness values of spring models from the Hounsfield units of a CT image. Similar reasoning [141] was applied for the recovery of the Young's modulus of bones from CT scans. Brain MRI images could be used to approximate the stiffness of brain tissues since its compliance has been shown to be correlated with water content of in vivo brain tissue. Experiments that are more accurate have been reported by Manduca et al. [142] using magnetic resonance elastography (MRE). By propagating acoustic strain waves, MRE images provide an estimate of elastic stiffness for small displacements.

3.2.2. Efficient computation

Computation time is an important constraint for surgery planning or surgical procedure simulation. To achieve a given computation rate, it is necessary to make a compromise between the mesh resolution and the complexity of the biomechanical model. The exponential increase in computing and graphics hardware performance should lead naturally to denser soft tissue models. However, the addition of more sophisticated models of deformation and interaction requires even more computation power. It is therefore necessary to develop efficient algorithms [124], specifically for the following three tasks,

1. deformation of non-linear viscoelastic tissue models;
2. collision detection between deformable bodies;
3. computation of contact forces between deformable bodies.

It is likely that improved algorithms will stem from the both biomechanics and computer graphics communities.

3.2.3. Medical validation

Validation of soft tissue deformation is a crucial step in the development of soft tissue modeling in medical simulators. It requires the comparison of deformations between computerized models and in vivo tissues. The shape variation of tissues can be measured through tri-dimensional imagery such as CT-scanners or MRI images. By combining image segmentation with non-rigid registration, displacement fields of tissues can be recovered and then compared with predicted displacements of soft tissue models. Physical markers or tagged MRI could help solving the matching problem. For a complete validation, the measurement of stress and applied forces on actual tissues should be performed and compared with predicted values through finite element methods or numerical calculations [124,143,144]. It is likely in the future that interaction between biomechanics and computer graphics will contribute to a major improvement in soft tissue modeling.

4. Computer aided tissue implantation

Computer aided tissue implantation covers topics on scaffold guide tissue engineering, computer model assisted surgery, and prototyping model assisted surgical planning.

4.1. Scaffold guided tissue engineering

Scaffolds used in tissue-engineering need to be biocompatible and designed to meet the nutritional and biological needs of the cell population involved in the formation of new tissue. In the scaffold guide tissue engineering, materials can be subdivided into natural materials such as collagen, hydroxyapatite (HA) or alginate and synthetic materials such as lactic-glycolic acid or polyacrylonitrile-polyvinyl chloride. Natural materials may be the actual in vivo extra cellular matrix components for cells, and as such would possess natural interactive properties such as cell adhesiveness [42,145]. Scaffold structure influences the behavior of ingrown cells and tissue structure. Performances of varied functions of the tissue structures depend on scaffold microstructures.

Scaffolds, however, are often limited in practical thickness due, in part, to the difficulty in getting cells deep into interior regions of scaffolds. This problem might be eliminated if cells could be simultaneously added to the scaffolds during the scaffold synthesis process. Although advanced manufacturing, such as solid freeform fabrication, has been adopted in the synthesis of tissue scaffolds [42,145–147], however, scaffold fabrication processes typically involve heat or toxic chemicals that would kill living cells and limit to incremental build-up the advanced bioreactor. To address these issues, new manufacturing process is under the development so that the syntheses of scaffold can not only have a controlled spatial gradients or distributions of cells and growth factors, but also a controlled scaffold materials and microstructure. For example, other than using solid modeling and B-rep modeling approach to design, characterize, and visualize tissue scaffolds, using solid free from fabrication process to built prefabricated cross-sectional layers of scaffolding seeded with cells and/or growth factors and stacked them up with biodegradable or non-biodegradable fasteners to form 3-D tissue structure was also reported [42].

4.2. Modeling based computer assisted surgery

Computer assisted surgery is a relatively new field that has made a great impact on medicine in the last few years [37,38]. The advantages of using patient internal anatomy in 3-D prior to perform surgery are obvious. Much of the challenge of surgery relies on clearly understanding the relative positions or critical vascular, neural, and other structures in the context of the adjacent or enveloping hard and soft tissue anatomy. Since much information by the classic anatomy study via dissection is difficult to obtain, the surgeon relies heavily on radiological imaging to provide an indication of the patient unique 3-D structure and computerized models and prototyping models to assist surgery [148,149].

Reference [150] presents some advantages of using computer medical modeling in craniomaxillofacial surgery.

1. The models outline the anatomy and avoid intra-operative 'surprises', especially on patients who have had many previous operations.
2. The use of a model decreases the operation time significantly by allowing the surgeon to practice and eliminate many of the technical imperfections and difficulties that are usually encountered intra-operatively.
3. The soft tissue is not an obstacle to skeletal exposure; therefore, the model surgery can be performed more accurately, setting the stage for a more precise in vivo operation.
4. Model surgery adds to the experience of otherwise less experienced cranio-maxillofacial surgeons.
5. Model surgery provides an ideal setting for the education of residents and colleagues, and possibly for the patient in carefully selected circumstances.
6. A post-operative model repeated at a later date is an accurate way of accessing surgical outcome and with repeated models one can

assess perfectly the long term results and changes.

7. Models created over an extended period provide an opportunity for methodical observation of evolutional changes in the craniomaxillofacial deformity as well as normal growth patterns.
8. In dealing with extensive bone tumors, a model gives precise definition of tumor extent, and enables the surgeon to plan the reconstructive approach pre-operatively.

In general, computer medical modeling can be used in assisting following surgical application.

4.2.1. Surgical planning

Computer model can be used as the communication tool between medical staff, the patient, and the design of individual implants and prostheses. Surgical planning tries to minimize the duration of surgery to reduce the risk of complications [123]. Normally, surgeons use imaging modalities like conventional radiographs, CT and MRI for supporting the planning process. RP plays an important role in surgical planning. It is particularly valuable when the anatomy is distorted. A precise RP model facilitates the pre-operative planning of an optimal surgical approach and enables visualization of complex anatomical architecture and correct pre-selection of appropriately fitting implants [38]. Surgeons are able to rehearse the fitting of the implants on the RP model prior to operating on the patient, to evaluate the results of, and gain confidence in, the planned approach thereby reducing costs and saving time by replacing the physical models.

4.2.2. Pre-operative planning

Computer model provides a general outline but more specific decisions, e.g. the exact position of the osteotomy lines are often postponed. These needs to be determined during the operation and this drastically increase the operation time [37]. This enhances the risk, especially for infants treated in this manner.

4.2.3. Modeling simulation

Modeling simulation is used to manipulate, (1) images generated from CT scans; and (2) mathematical model or CAD-based medical model [151,152]. There are three types of functionality which have to be integrated into the modeling simulation algorithm, (a) the accurate representation of biological structures by the computer modeling; (b) be possible to simulate all surgical actions; and (c) capable of obtaining certain parametric information such as tissue volume and anatomic distances.

4.2.4. Intra-operative assistance

Intra-operatively, computer modeling can help with the navigation of instruments by providing a broader view of the operation field. In combination with robotics, it even can supply guidance by pre-defining the path of a biopsy needle or by preventing the surgical instruments from moving into harmful regions [123].

4.3. Prototype modeling assisted surgical planning

Although rapid prototyping technology has been exploitatively used in assisting surgical planning and 3-D reconstruction, it is still in its infancy in the biomedical application. Precise description of quality requirement for medical models produced through different RP processes for various surgical applications are immediately needed. Fulfillment of different quality feature of RP models in clinical practice for bone surgery is required. Evaluation on quality requirements for accuracy, surface detail, transparency, color, size, disarticulation, mirror models, rigidity, temperature resistance, toxicity, production time, and price need to be conducted before we can provide convincing evidence for the US insurance companies that RP technology is ultimately a cost saving measure in the medical application.

RP technology produces extremely detailed models that serve as excellent templates for the creation of custom implants. For multi-copy production or production in special materials, conventional machining with cutting mills either can directly create metal molds suitable for casting or can produce models out of a material suitable for casting. Solutions are being sought in both new materials and new fabrication methods that produce relatively porous and hence removable models. RP technology also faces challenges in the direct creation of biocompatible implants. Conventional machining can be used to fabricate implants from hydroxyapatite-based materials that allow for the in vivo, direct osseous replacement of the implant. Some RP technology processes, such as laser sintering might be adaptable to bioreplaceable materials.

The advantage of RP technology is complete visual appreciation of bony anatomy hitherto unavailable. The modeling process is very accurate, reproducing CT data to a tolerance of 0.1 mm. The major source of error is the CT scanning process itself, where inaccuracies of up to 1 mm can occur. Thus, medical imaging is the limiting factor when producing RP bone models. The obvious application of this technology is in bone surgery, for example, where the orthopedic surgeon can be challenged by complex congenital deformity, traumatic reconstructive procedures or joint vision surgery. RP technology models allow surgery to be accurately planned, osteotomy cuts can be practiced on the model, plates may be preformed and prostheses such as implants custom made to each individual patient. The advantage of planning and practicing the procedure in vitro should be reduced operating time and improved results.

5. Conclusion

This article presents a review of recent developments in CATE in following three applications, (1) computer-aided tissue anatomical modeling; (2) computer-aided tissue classification; and (3) computer-aided tissue implantation.

Although, the advances in diagnostic imaging have meant that less reliance is now placed on the interpretation of clinical signs and symptoms, the very real advantages offered by the imaging techniques make them indispensable to modern surgical practice and further refinements in the field of 3-D imaging with all modalities have made their use even more appealing. Imaging technologies, CT/MRI, have greatly enhanced 3-D anatomy visualization, which is the key step in 3-D reconstruction. Three-dimensional reconstruction has led to the formation of 3-D physical biomodels, which greatly facilitates characterization, analysis and simulation of tissue structures. Tissue classification has now been revolutionized with the use of computer technology. Classification is useful in trauma identification, tumor diagnosis, lesion area measurement and its structural analysis. Computer aided tissue implantation facilitates the development of tissue scaffold modeling, its prototyping modeling and surgical planning.

With future improvements in computer software and materials, models having greater accuracy and lower cost may increase their role in CATE. In the near future, 3-D imaging will be integrated in surgical suites with MR imaging instrumentation. These MR imaging surgical suites will allow surgeons to probe tissue intra-operatively and view detailed soft-tissue anatomy in real time while performing interventional procedures. The real-time reconstruction's will provide a 3-D view of anatomy utilizing probes for both localized 3-D image collecting and treatment.

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