Digital hand atlas and web-based bone age assessment: system design and implementation

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Abstract

Bone age assessment is a procedure frequently performed in pediatric patients to evaluate their growth disorder. A simple method commonly used in bone age assessment is atlas matching by a radiological examination of a left-hand radiograph against a reference set of Greulich–Pyle atlas patterns of normal standards. The method however can lead to significant deviation in age assessment, due to a variety of observers with different levels of training. The Greulich–Pyle atlas developed in the 1950s based on middle upper class white populations, is also not fully applicable for children of today, especially regarding the standard development in other racial groups.

In this paper, we present our system design and initial implementation of a digital hand atlas and computer-aided diagnostic (CAD) system for Web-based bone age assessment. The CAD system is built on top of existing picture archiving and communication system (PACS), as well as recent advances in Internet technology. It consists of a hand atlas database, a CAD module and a Java-based Web user interface. The digital atlas is based on a large new set of clinically normal hand images of diverse ethnic groups. A relational image database system is used to organize hand images, their extracted quantitative features and patient data. The digital atlas removes the disadvantages of the currently out-of-date Greulich–Pyle atlas and allows the bone age assessment to be computerized. The Java-based Web user interface allows users to interact with the hand image database from browsers. Users can use a Web browser to push a clinical hand image to the CAD server for a bone age assessment. Quantitative features on the examined image, which reflect the skeletal maturity, are then extracted and compared with patterns from the atlas database to assess the bone age. The digital atlas method based on open system Internet technology provides an alternative to supplement or replace the traditional one for a quantitative, accurate and cost-effective assessment of bone age.

1. Introduction

Bone age or skeletal age assessment is a procedure performed in pediatric patients to evaluate their growth disorder, determine their growth potential, and monitor the therapy effects of growth. The growth potential of an individual depends largely on the progression of ossification within the epiphysis. Bone age is a measurement of the epiphyseal center development. It is an important procedure in the diagnosis and management of endocrine disorders, diagnostic evaluation of metabolic and growth abnormalities, deceleration of maturation in a variety of syndromes, malformations, and bone dysplasias.

A simple method frequently used in bone age assessment is atlas matching by a radiological examination of a left-hand and wrist radiograph against a reference set of atlas patterns of normal standards. Although the hand and wrist does not contribute to the height of an individual, the radiograph of this part of the body has been proven valuable and is commonly used in assessment of bone age. The reference set of patterns currently used extensively is Greulich and Pyle [1] atlas that includes one hand image pattern per year of age. The pattern in the atlas, which appears to resemble the clinical image, is selected. Since each pattern in the atlas represents a certain year of age for a normal child, the selection assigns the patient’s bone age. The difference between the assessed bone age and the chronological age indicates abnormalities in patient’s skeletal development.

The hand atlas matching method is universally used due to the advantages of simplicity, minimal radiation exposure and the availability of multiple ossification centers for evaluation of maturity. The method, however, is mostly qualitative and not accurate. It is liable to deviations by
subjective nature of various observers. Furthermore, the atlas itself, which was developed by Greulich and Pyle [1] in 1950s based on middle class white populations, is not fully applicable for today’s children especially regarding the standard development in other racial groups [2–4].

Many efforts have been made to increase the accuracy of the bone age assessment and to overcome the ethnic and racial differences in skeletal maturation. The Tanner and Whitehouse [5] (TW2) method is base on assigning an individual score to several bones in the hand and wrist, and then obtaining the bone age by the total score. Schmid and Moll [6] developed standards for the German population, Eklof and Ringertz [7] devised a method for evaluation of maturation based on the bone length and width of the Scandinavian people, and Sugiura [8] has published standards for both sexes for Japanese children.

The computer-aided methods have also been under development to quantify radiological findings that may support the bone age assessment [9,10]. The Tanner–Whitehouse (TW2) scoring method has been computerized by performing the Fourier transform on radiographs digitized by a video camera [11]. The method is quite tedious and time consuming to perform. Pietka and Huang [12] started seven years ago a computer-assisted analysis in bone age assessment and have since then conducted a series of studies on bony feature extraction by image processing [13–16]. They first identify the regions of interest (ROI) that are the most significant in bone age assessment, i.e. the phalanx, epiphyses and carpal bone areas as marked in Fig. 1, and then apply variety of image processing techniques to extract the quantitative features associated with these ROIs. These computer-extracted parameters are associated with race, age, sex and Tanner maturity index [17], providing a valuable means of quantitative measurements that form the basis for computer-assisted bone age assessment.

The greatest impact of a more accurate, objective, and reproducible technique for assessing skeletal maturity would be in refining the treatment for certain endocrine and musculoskeletal diseases. The evaluation of the response to growth hormone, for example, is particularly
imprecise. A computerized analysis of a patient being studied on multiple occasions during therapy could simultaneously provide a determination of bone age and a detailed report of the changes from one study to another. In patients evaluated for surgery to correct scoliosis or leg-length discrepancy, inaccuracies in bone age determination can lead to mistakes in the timing of the surgery. Scoliosis does not usually progress after the patient is skeletally mature; a misdiagnosed bone age determination can lead to unnecessary surgery if the bone age is underestimated, or premature intervention if the bone age is overestimated. In the case of leg-length discrepancies, incorrect timing of corrective surgery can result in insufficient or excessive therapy, both of which can result in deformity and disability.

We have been in a process of constructing a digital hand atlas since 1997. The digital hand atlas built on a hospital-integrated picture archiving and communication system (PACS) can overcome the shortcomings of the traditional atlas. Building a current and clinically useful atlas is a tedious process. Large set of images along with all relevant patient data have to be accumulated over the years, constantly maintained and replenished with new materials. It is possible to do that only when the atlas is built under the PACS environment [18,19] and integrated with the hand image acquisition machines such as CR (computer radiograph), in which digital images and relevant patient data can be easily selected and incorporated into the atlas. The digital atlas manifests itself in an image database, consisting of a large set of 1120 high-resolution reference images with computer-extracted bone objects and quantitative features. It would grow over time, allowing a continuous accrual of normal standards and improving the assessment accuracy of bone age.

To make the digital atlas widely available to and easily accessible by clients, a thin-client distributing environment such as the Web is a preferred development and deployment platform that might otherwise be limited to only a few local workstations. The Web technologies have progressed from a static simple Web page to dynamic one including whose content is built on the fly when a user requests it. Major database vendors have also implemented the Web technology into their database products for interactive database query through Web. In other words, rather than loading the huge atlas database (about 10 Gbytes in size) and its software package on every client's machine, people will use common Web browsers to interact with the atlas. The Web browser will take care of most of the user-interface concerns and allow us instead to focus on the computer-assisted diagnosis (CAD) model of encoding work flow and linking of appropriate task-specific modules/tools on the server side. With the maturity of PACS technology and recent advances in open system Internet technology, we will be able to develop a large and sharable hand atlas as a clinical reference and use the Web as a delivering platform. Clients will use widely available Web browsers to browse the digital atlas, view the hand images and push clinical images to the web server for automatic bone age assessment.

In this paper, we present the system design and integration, a Web-based client–server model for computer-aided bone age assessment and our initial implementation of the digital atlas database.

2. System architecture for the digital hand atlas

Fig. 2 shows the system architecture and the building blocks for a digital hand atlas in a Web-based environment [20]. It includes the collection of hand images and their relevant patient data, the hand atlas database and server, and the Web interface. This architecture can also be described in the framework of CAD in a PACS environment [18,19]. PACS has evolved into a hospital-integrated information system with a voluminous amount of image and associated data in its database. Integrating of the CAD in a PACS environment can facilitate the usefulness of CAD in medical practice and take advantage of the already available resources in PACS, such as image storage, retrieval mechanism and communication network.

The digital atlas server is to extend clinical-oriented PACS for CAD purposes. The extension takes the form of the server hosted on a machine separated from PACS. It is important to build a separate server for handing the CAD modules so as not to impact the performance of PACS in its fulfillment of high-priority tasks of supporting day-to-day radiological services. The acquisition workstation and the database server are Digital Imaging and Communications in Medicine (DICOM) compliant. Both have been implemented [21] on the Sun SPARC Ultra-II platform. The hand image acquisition has been standardized as shown in Fig. 3. All hand images along with their relevant patient information are retrieved through the acquisition computer, automatically transferred to and stored in the RAID disks, and then inserted into our newly established atlas image database.

The digital atlas server, currently hosted on the Sun SPARC Ultra-II platform, uses a thin-client 3-tier architecture— atlas database, CAD application and Web servers. It allows open
access from Web by clients running in Unix, PC or Macintosh. The digital hand atlas is an image database managed by Oracle relational database server. The Application Server acts as a platform for reusable logic, taking responsibility for application code that might otherwise reside at the client or the database server. It contains the image processing and CAD bone age assessment modules, bringing together the Web with the digital atlas database. It also provides other middleware functionality such as quality service (scalable, reliable, secure, and manageable), tight database integration, easy migration of legacy applications and reliable transactions for network clients.

3. Data collection

The first step in generating the atlas is to select left hand and wrist images either computed radiography (CR) or digitized film images, from healthy normal children. The normal reference images are categorized according to the ethnic origin and sex since these two factors have the most effect on bone growth. Based on our previous estimation [15], for pre-pubertal children 5 images for each group would be needed to detect a difference between manual and computer-assisted measurements of the distal, middle, and proximal bones. Whereas, for children during puberty, 10 images at each group would be needed to detect a difference between manual and computer measurements. Consequently, 140 reference images are needed for each race—sex group from normal newborn to 18 years of age. Total of 1120 reference images (140 × 8 groups) is going to be collected from boys and girls of European, African, Hispanic, and Asian descent. As an example, Fig. 4 shows the database query result summarizing the currently collected reference images for the African American female group.

The information obtained from this data set would overcome the scarcity of studies assessing the differences between skeletal and chronological age in nonwhite children in this country, and will cover the entire range from birth to skeletal maturity. This is the only study, to our knowledge, that analyses the differences between skeletal and chronological age for children, of various ethnic backgrounds of the 1990s from birth to skeletal maturity.

As of today, over 500 normal hand images from newborn to 18 years have been selected at Children Hospital of Los Angeles (CHLA) by Dr Gilsanz. The reference hand images have been and will continue to be selected at CHLA by Dr Gilsanz. He and his colleagues recruit, interview, and examine the local children to obtain the left hand and wrist images, which are considered to be clinically normal and standard. All relevant patient information, including the chronological age, date of birth, date of examination, race, sex, height, weight, trunk height and Tanner maturity index have also been collected. The films (if not CR) are forwarded to and digitized at UCSF with a film scanner (Abe Sekkei Inc., Japan) to 100 μm sampling distance and 12 bits resolution. Both CR and digitized images are first assured of the quality and then transferred to the atlas server for computer-assisted bony feature extraction. The images along with their pertinent patient information and extracted bony objects will then be indexed into an image atlas database.

Meanwhile, the daily clinical bone age assessment cases, which use the traditional Greulich and Pyle method, are collected locally at UCSF. About 400 left-hand images along with relevant information from selected patients who came to the UCSF for clinical bone age assessment have been retrieved from the UCSF PACS/RIS systems. The bone age assessment cases at UCSF continue at a rate of 25 cases per month. This clinical data set will be used for checking and refinement of the digital hand atlas, comparing the conventional method with the digital atlas CAD method.

4. Atlas database development

The digital hand atlas is a medical image database currently managed by Oracle 8i data server (http://www.oracle.com/database/oracle8i Oracle Corporation, Redwood Shores, CA). Oracle 8i is the Oracle’s newly released database specifically designed to manage the new medium
of the Internet in addition to supporting traditional relational data. We have further extended and customized the Oracle 8i data server to manage medical image data, including high-resolution hand images, their bone objects and their relational dependencies. The data server will also support assessment of skeletal maturity in clinical diagnosis and research. One of the greatest barriers to medical information systems is the integration of all patient data—including images—into an intelligent image database [22]. New tools are required not only to store clinical information together with high-resolution images, but also to provide radiological findings describing the stage of skeletal development and use them together with clinical data for the final assessment of the developmental stage of the patient.

Building a current and clinically useful hand atlas for various ethnic groups is a tedious process. Large standard set of normal hand images along with all relevant patient data have to be accumulated over the years, constantly maintained and replenished with new materials. It becomes possible and also cost-effective when the atlas is built under a PACS environment from which new images and relevant patient data can be easily selected and incorporated into the digital atlas to increase the statistical power of the CAD. In this case, when a pediatric patient comes in for hand X-ray examination and is determined as normal, then the image...
and related data can be query/retrieved through the PACS database and downloaded to the digital hand atlas database. The atlas database will provide an information infrastructure for clients to access, correlate, query, and organize all the patient hand and wrist radiographs. It is based not only on traditional medical records but also on hand image contents, such as bone objects extracted from phalangeal (PROI), carpal bone (CROI), and epiphyseal (EROI) regions of interest. It can access and manipulate regions of interest in images defined in object data model as a relation database system does for arbitrary portions of data defined in records and tables. Making the case for medical image databases must also require addressing it as a long-term system, not a one-shot event. Thus, the atlas database development and management will provide:

- Integration of image data and radiological finding with the traditional texture-based database.
- Structural objects of image segments representing the regions of interest in a hand image.
- Relationships among medical records and verity of bone objects.
- Feasible way of classification, to map the bone objects to bone age.
- Modular implementation, to allow a modified (extended) structure of data record to be built on and to complement what already exists so that the database developed is a dynamic process. Additional normal hand images can be appended to increase the sample size and new discriminatory features can be introduced to improve the statistical power of the database.
- Portability of the methodology and software across various computing platforms from a large-scale PACS to a minimum configuration with a digitizer and a workstation allows the outcome of the project to be implemented in other clinical settings.

Fig. 5 shows the currently implemented database tables representing hand data structures following the above atlas design guidelines. The atlas table contains all relevant textual data of a patient hand image. It is indexed by a group ID and an image file name. A group ID such as BLKF12 uniquely determines the race (BLK), sex (F) and year of age (12)-three key elements in classifying a patient’s bone age. The image name in the table points to a high-resolution hand image stored offline outside of database.

5. Bone age CAD server

As the Web has evolved from its origins as a simple delivery mechanism—suitable for small files and applications—to a platform for complex applications and dynamic database publishing, Web servers and Web technology have not, in general, kept pace. A Web-based medical application such as our digital atlas and bone age assessment demands new robust, scalable architectures and a new class of servers, acting as a middleware to support a large image size, complicated image process, distributed and heterogeneous application environment. The middleware application server acts as a platform for reusable logic, taking responsibility for application code that might otherwise reside at the client or the database server. In the case that the digital hand atlas is used for Web-based bone age assessment, the application server contains the image processing and CAD bone age assessment modules. The application server brings together the Web technology with the digital atlas database. It also provides other middleware functionality such as quality service (scalable, reliable, secure, and manageable), tight database integration, easy migration of legacy applications and reliable transactions for network clients.

We currently use Oracle Application Server 4.0 (Oracle Corporation, Redwood Shores, CA) as an integration platform to host our server-side software/tools packages. These packages have been developed in variety of programming languages and image libraries for image acquisition, processing, managing and display. The CAD model will encode
workflow and link task-specific tools on the server side, specifically for the following:

Image acquisition: Image acquisition software is built into the CAD atlas server. Hand images can be transmitted from an independent CR or film digitizer to the atlas for bone age assessment. DICOM client software as well as its Web interface will also be integrated into the CAD server. The users can retrieve from the digital atlas the hand images and corresponding child data as a reference through the Web. Meanwhile, a user can send in a request to retrieve a patient hand image from a remote DICOM compliant PACS for online bone age assessment on the CAD server.

Image processing: The CAD server provides many image-processing services that are computationally intensive operations, thus reducing the hardware and software requirements on the client’s machine. The services include image format conversion from and to the standard DICOM format, image background removal to eliminate the useless area in the radiograph, and image feature extraction and classification for bone age assessment. The services also include image manipulation functions, such as image compression, scaling, and pre-defined window-level-gamma adjustment so that the best image display quality will be achieved on a remote client’s monitor without manual intervention. The image processing packages have been developed on the Sun Solaris platform with image libraries Matlab (MathWorks, Inc., Natick, MA.), XIL (X Image Library, Sun Microsystems, Mountain View, Calif.), variety of commonly available free image libraries, as well as several in-house programs specially for bone age assessment [15].

Web-based bone age assessment: Fig. 6 shows a work-up sequence for a Web-based bone age assessment and illustrates the role that the CAD server plays between the Web server and the digital atlas database. A patient hand image to be examined will be pushed in through the Web server. The image is passed on to the CAD server for pre-processing and feature extraction. The radiological findings associated with the extracted bony features are then compared with corresponding values from the hand atlas database and therefore to determine the patient’s bone age. An assessment report along with relevant hand images is then sent back to the client’s browser through the Web server.

Data security: Bone age assessment across open network raises an important security issue of privacy, authenticity and integrity for sensitive medical image data. To ensure security, we will implement three levels of measures in the digital atlas system. The first level is provided by the Oracle application server, which supports the following:
- Secure Sockets Layer (SSL) Version 3, which addresses this problem by scrambling data sent from the server to browsers in such a way that only the browsers can unscramble the information when they receive it. Any intermediate computers involved in routing the information see only gibberish that they cannot decipher. SSL is an emerging standard for secure data transmission over the Internet.
- Basic and digest authentication schemes, which prompt the user to enter a user name and password before processing the user’s request.
- IP-based and domain-based restriction schemes, which allow access to files only if the client is from a list of IP addresses or domain names.

The second level is to use a firewall to secure the hand atlas server. The firewall will be placed in front of the Web server. In this case, the firewall provides access for browser to Web server communication, and allows secure HTTP and SSL protocols to pass through.

The third level is to embed encrypted digital signatures onto a digital hand image. These digital signatures are based on certain characteristics of the hand image and patient-related information. The embedded information can be extracted and decrypted by the receiving site to verify the authenticity of the sender as well as the integrity of the image and patient information, which are not available in the previous two levels of securities. We will develop a digital signature scheme based on the techniques we implemented for digital mammography [23].

6. Java-based Web user interface

Java is a platform-independent programming language. We will develop a Java-based user interface for browsing the digital atlas and for online bone age assessment. The
interface written in Java, known as a Java applet, can be automatically downloaded to and executed from user’s web browsers without requirement of additional software installation on client sides. It facilitates the use of Web browsers to navigate the digital hand atlas and manipulate images interactively using any common computer systems. Meanwhile, the interface written in Java language can also serve as a standalone application, which can be distributed along with the atlas and installed on clients’ machines in case there is no dedicated network connection to the atlas server.

The Web-based paradigm is essentially a request/response model. The Web browser takes care of most of user-interface concerns, rendering the Web pages dynamically formed on the fly by procedures in the digital atlas server. The server procedure first generates an Hypertext Markup Language (HTML) login form as shown in Fig. 7. The user’s login typically will result in a Web-to-database procedure that determines the user’s privilege and role. The server then sends back to the user an HTML main page containing hot links, on each of which the user can click on to perform a specific task.

When the user clicks on a link requesting an on-line bone age assessment, the Web server sends back a form, similar to the one in Fig. 7, for uploading clinical hand images. The user can upload the images from a local hard disk to the server simply by dropping the image files from their window file manager to the uploading window or from another remote server by specifying a Uniform Resource Locator (URL) address for the CAD server to fetch. Upon receiving the hand images and patient data from either the DICOM compliant PACS or a stand-alone image acquisition device, the server will call a procedure, illustrated in Fig. 6, to do feature extraction from the uploaded hand image and interact with the digital atlas database for bone age assessment. The assessment report will be formatted in HTML and sent back to the user. The report contains assessment results, thumbnails for accessing full-size hand images and links to manage records in the user’s private database.

A user can also interactively query and browse the digital hand atlas database via web. Fig. 8 shows an example of Java applet for accessing reference hand images and their relevant information. An atlas query form at the top shows the image groups based on race, sex, age and other essential group information. The query form provides an easy way for a user to select an interesting group from the atlas. The records under the queried group are listed with their relevant patient information—age, date of birth, date of examination, height, weight, trunk height and Tanner maturity index. At the bottom are the thumbnails that can be selected and clicked on to display a full-size hand image. The selected image will then be displayed on a separated image display window similar to one in Fig. 1.

Fig. 1 is a screen shot of the left hand and wrist image. A platform-independent image viewer based on Java technology will be developed to handle full-size image display. The image is first displayed at a reduced resolution to fit the window since the full resolution hand images (\(2 \times 2.5K\)) from older children groups are too big to display on the regular computer monitor. This permits images of various age classes to be displayed for an easy preview. The reduced image can be expanded to full resolution one with a vertical and a horizontal scroll bar to control the viewing window. The image tools will include window-level adjustment, gamma correction, scroll, scaling and zoom, and image comparison.

A demonstration of Web-based atlas browsing and bone age assessment has been set up at http://boneage.lri. ucef.edu.

7. Distribution and Web deployment of the digital hand atlas

The digital hand atlas will be available to other hospitals, as a reference standard for assessment of bone age. The atlas server will be in our laboratory (Laboratory for Radiological
Informatics) at UCSF. The clients at the other sites can use a commonly available Web browser on any computer platform to access our digital atlas server for bone age assessment. There is no need for any additional software installation or management on clients’ sides. The atlas and all its relevant software packages reside on the server. Real-time atlas image browsing and bone age assessment needs a dedicated network connect at speed faster than 10 Mbits/s so that a full-size hand image (average 6 Mbytes in size, 3 Mbytes lossless compressed) can be displayed in less than 8 s. Meanwhile, the image processing and bone age assessment on the server side takes about additional 3–5 s. We formulate the following procedures for bone age assessment via Web, based on the network speeds.

- Real-time atlas browsing and bone age assessment (network speed >10 Mbits/s): Potential Sites
  1. PACS workstations and radiology reading rooms at UCSF via LAN. All current PACS workstations at UCSF are able to communicate with our servers over either asynchronous transfer mode (ATM) OC-3 at the speed of 155 Mbits/s [24] or fast Ethernet at 100 Mbits/s.
  2. UCSF, MZH, SFVA and SFGH in the San Francisco Bay Area. The four sites shown in Fig. 9 are
This paper presents the system architecture for a digital hand atlas with a large reference set of normal hand images and the methods to implement a Web-based computer-assisted diagnostic system for bone age assessment. The architecture is built on top of existing clinical information system and current Internet technologies. It illustrates the potential of these cutting-edge technologies in medical informatics, and provides a new, cost-effective and convenient way of assessing bone age.

This is an ongoing project. Currently we are refining the algorithms for bone feature extraction, fully integrating system components and building Java-based Web interface. By the end of this study, there will be a medically accepted standard hand atlas able to be used as a reference. The digital atlas will be constantly updated and replenished with new materials, removing the disadvantages of the currently used one, incomplete and out-of-date. A computer-assisted image analysis will permit the diagnosis to be standardized and become more objective and reproducible. A Java-based Web interface provides a platform independent, cost-effective, and widespread means to assess the bone age.

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References


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