RheumaSCORE: A CAD System for Rheumatoid Arthritis Diagnosis and Follow-Up

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Abstract. Recently, computer-aided diagnosis (CAD) has become one of the major research subjects in medical imaging and diagnostic radiology. The goal of a CAD is to improve the quality and productivity of physicians' job by improving the accuracy and consistency of radiological diagnosis. This paper describes RheumaSCORE, a CAD system specialized for the diagnosis and treatment of patients affected by bone erosions, as a consequence of one of the most common and serious forms of arthritis, the Rheumatoid Arthritis (RA), and gives an overview of its main features.

Keywords: Computer aided diagnosis (CAD) · Rheumatoid arthritis · Medical imaging · Erosion scoring · Rheumascore

1 Introduction

With the rapid advances in computing and electronic imaging technology, there has been an increasing interest in developing *Computer Aided Diagnosis* (CAD) systems to improve the medical service. CAD is emerging as an advanced interdisciplinary technology which combines fundamental elements of different areas such as digital image processing, image analysis, pattern recognition, medical information processing and management. This technology can be applied to all imaging modalities, including projection radiography, computed tomography (CT), magnetic resonance imaging (MRI), ultrasound (US) and nuclear medicine imaging (PET, SPECT), used for all body parts and for all kinds of examinations.

Although current CAD systems cannot fully replace human doctors for medical detection/diagnosis in clinical practice, the analytical results will assist doctors in providing functionalities for diagnosis, treatment, adequate follow-up, and timely monitoring of disease indicators [1,2,3,4,5].

This paper provides an overview of the main functionalities of the RheumaSCORE CAD system [11], specialized for the diagnosis, quantification and monitoring of one of the most common consequence of musculoskeletal diseases (MSD) like the Rheumatoid Arthritis (RA), the bone erosions of the wrist and hand district, through their automatic quantification using the OMERACT-RAMRIS method [30].

RA is one of the most common and serious forms of arthritis. It can lead to long-term joint damage, resulting in chronic pain, loss of function and disability. This chronic

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disease affects about 2.9 million people in Europe [24,25]. An early diagnosis, the continuous monitoring of disease activity and the constant evaluation of therapy effects can improve patients' quality of life and may reduce related social costs. MRI has been demonstrated to be two to ten times more sensitive than conventional radiography in detecting wrist erosions in RA, especially in its early phases [26]. In general, erosions detectable on MRI may become visible in x-ray images only 2-6 years later [26,27,28,29].

The wide use of MRI in the assessment of joints in RA patients in the last years emphasizes the need for an objective and reproducible scoring system of RA lesions. An international working group developed a MRI scoring system to assess both inflammation (activity) and bone lesions (damage) in RA patients based on the Outcome Measures in Rheumatology Clinical Trials (OMERACT) [30].

Manual evaluation of bone erosions volume is however tedious, time consuming and not fully repeatable (especially for inexperienced users). Considering the big amount of patients suffering from RA, this is a critical task. The *RheumaSCORE* software was developed by Softeco Sismat S.r.l. to face the RA problem [11,12], [31].

The paper is organized as follows. In Section 2, the state of the art of CAD systems will be described with focus on segmentation and erosion evaluation techniques in literature. In Section 3, RheumaSCORE and its main functionalities will be presented and some clinical trials will be discussed.

2 State of the Art

2.1 CAD Systems

Early studies on quantitative analysis of medical images by computers [15,16,17,18,19,20] were reported in the 1960s. At that time, it was generally assumed that computers could replace radiologists in detecting abnormalities, because computers and machines are better at performing certain tasks than human beings.

In the medical subspecialty of hematology, R.L. Engle [21] stated in the conclusion of his review article on 30 years' experience in using computers as diagnostic aids in medical decision making, that the computers cannot replace the physicians, but only support them during the diagnostic process. This awareness was already confirmed in the 1980s, when another approach emerged which assumed that the computer output could be utilized by radiologists, but not replace them. This concept is currently known as computer aided diagnosis, which has spread widely and quickly.

A large number of CAD systems has been employed for assisting physicians in the early detection of cancer (breast tumors in mammograms [6], lung nodules in chest radiographs/CT [7], colorectal polyps in CT colonography [8]) and intracranial aneurysms in magnetic resonance angiography (MRA) [9].

In the context of RA, Kubassova et al. [10] developed a CAD software for semi-automated and automated quantitative analysis of dynamic contract-enhanced MRI (DCE-MRI) data, DYNAMIKA. This CAD incorporates algorithms for the estimation of various inflammation such as the one related to the synovial activity in RA. Peloschek et al. [22] developed a software that allows a fast, accurate, and reliable documentation of erosive and degenerative changes on radiographs of hands, wrists, and feet in RA.

The current trend of the research in this field is the development of CAD systems assembled as packages, associated with some specific imaging modalities such as digital mammography, CT, and MRI, and implemented as a part of PACS (Picture Archiving and Communication Systems). For example, one of the potential advantages in packaging a CAD in the PACS environment is the comparison between images and related measured data acquired in different times (follow-up). Another potential advantage is the use of similar cases in practical clinical situations: a unique database that includes a large number of cases which can be used as a tool for finding cases similar to an unknown one (knowledge management). In that sense, a first result for MSD application is the RheumaSCORE software [11,12], a specific CAD for RA.

2.2 Segmentation

The most important functionality of the CAD systems for supporting evaluation of RA within the wrist/hand joints is the segmentation. Segmentation is an important task in medical imaging, in order to recognize anatomical or pathological structures and determine their relevant characteristics such as size, shape, and volume. Moreover, image segmentation is the prerequisite for many interaction techniques to explore data and to carry out treatment planning.

In the context of RA, there is relatively few work on segmentation of wrist bones in 3-D MRI sequences. Sebastian et al. [13] describe an approach to segment carpal bones from computed tomography (CT) sequences using skeletally coupled deformable models. Similarly Duryea et al.[14] describe their semi-automated approach using CT data. Koch et al. [32] and Włodarczyk et al. [33] developed wrist segmentation framework on 3D MRI images. However, to the best of our knowledge, there is no commercial framework for wrist/hand segmentation designed for MR images.

2.3 Erosion Evaluation

Although a diagnostic standard for assessing RA in MR images of wrist/hand is used for almost a decade, there is currently no commercial tool supporting automated evaluation of erosions within the wrist/hand joints. In fact, no comprehensive framework for automated evaluation of these lesions has been even published. Although recently there have been some efforts to develop quantitative methods of assessing RA-related changes and comparing them with RAMRIS outcomes [34,35], these efforts were essentially based on manual outlining of wrist bones or joints borders in 3D MRI of wrist. Although based on manual outlining, the results of Crowley et al. [34] and Chand et al. [35] demonstrated that RAMRIS-based assessment of RA can be possibly replaced with a computer-aided detection (CAD) tool for estimating the volumes of lesions.

3 RheumaSCORE

3.1 Main Functionalities

RheumaSCORE is a CAD that supports the user (e.g. radiologist or rheumatologist) during the diagnostic process and the management of RA progression, by means of analysis, visualization, measurement and comparison of MRI acquisitions of different patients. This application offers to the physician the most common features that a CAD system must offer to the user:

1. image processing/clinical data storage for detection, visualization and qualitative/quantitative evaluation of abnormalities;
2. comparisons among images and clinical data of the same patient;
3. quantitative evaluation and retrieval of cases similar to those of unknown lesions.

3.2 Bones Segmentation

In RheumaSCORE the bones segmentation is performed using a semi-automatic segmentation algorithm based on level-set method [36]. The level-set method developed evolves a surface implicitly by manipulating a higher dimensional function, called the level-set function $\phi(x,t)$. The evolving surface can be extracted from the zero level-set $\Gamma(x,t) = \{(x,t) | \phi(x,t)=0\}$ with $\phi: R^n \rightarrow R$. In the level-set framework, one can execute a wide variety of deformations by introducing an appropriate motion function $\upsilon(x,t)$ of the surface. For segmentation, the $\upsilon(x,t)$ often consists of a combination of two terms [37]

$$\frac{\partial \phi}{\partial t} = |\nabla \phi| \left[\alpha D(x) + (1-\alpha) \nabla \cdot \frac{\nabla \phi}{|\nabla \phi|} \right] \tag{1}$$

where D is a data term that forces the model toward desirable features in the input data, the term $\nabla \cdot (\nabla \phi / |\nabla \phi|)$ is the mean curvature of the surface, which forces the surface to have a smaller area (and to remain smooth) and $\alpha \in [0,1]$ is a free parameter that controls the degree of smoothness in the solution.

The data function D (speed function) acts as the principal "force" that drives the segmentation. In our implementation, the speed function at any one voxel x is the result of the combination between two terms: $D_{intensity}$ and D_{fuzzy}. The first term $D_{intensity}$, based on the input gray value of the voxel x, is given by

$$D_{intensity} = \varepsilon - |I - T| \tag{2}$$

where T describes the dominant intensity of the region to be segmented and ε describes the range of grayscale values around T that could be considered inside the object. Thus, for a voxel x, the level-set propagation front will expand if the voxel intensity $I \in \{T \pm \varepsilon\}$, otherwise it will contract.

The second term D_{fuzzy} describes the fuzzy affinity between contiguous voxels. Affinity is intended to be a relation between every two image elements c and d. That is, if c and d are far apart, the strength of this relationship is intended to be zero. If the elements are nearby, the strength of their affinity, lying between 0 and 1, depends on the distance between them, on the homogeneity of the intensities surrounding them, and on the closeness of their intensity-based features to the feature values expected for the object. The strength of this relation, denoted μ(c, d), is given by

$$\mu(c, d) = k(c,d)\sqrt{g_1(f(c), f(d))\, g_2(f(c) f(d))} \qquad (3)$$

where k(c,d) has 0 or 1 value depending on c and d adjacency, g_1 and g_2 are Gaussian functions of (f(c)+f(d))/2 and (f(c)-f(d))/2, respectively. In this equation, g_1 is a Gaussian with mean and variance that are related to the mean and variance of the intensity of the object we wish to segment in the scene. That is, this affinity component takes a high value when c and d are both close to an expected intensity value for the object. g_2 is a 0-mean Gaussian, the underlying idea being to capture the degree of local hanging togetherness of c and d based on intensity homogeneity. For each voxel x, the term D_{fuzzy} is the mean value between the fuzzy affinity evaluated on the neighborhood of the voxel x. This term helps the level-set propagation front to evolve also in areas with different homogeneity intensity. Segmentation results are reconstructed in 3D and displayed using the Marching Cube algorithm [23]. More details and results of our segmentation method are described in [36].

3.3 Evaluation of RA Status and Progression

RheumaSCORE allows for the analysis of the bones in the hand and the wrist to assess the RA status through erosions scoring and progression monitoring. This evaluation is performed after segmentation using the same method proposed by OMERACT RAMRIS (see Fig. 1).

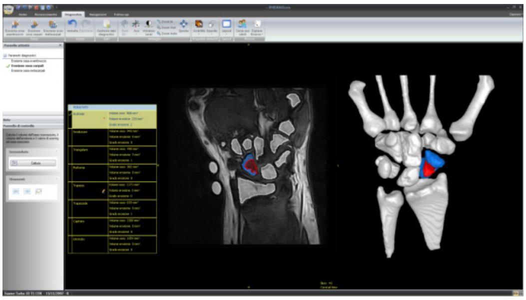

Fig. 1. Erosion Scoring in the RheumaSCORE software.

This method identifies and measures bone erosions, not segmenting directly the erosion, i.e. the missing part of the bone, but through the segmentation of the bone of interest and then the reconstruction of its original shape. RheumaSCORE uses a statistical shape model extracted from a collection of training samples of healthy bone. The resulting model consists of the mean shape and a number of modes of variation obtained with a Principal Component Analysis (PCA). Every healthy bone can be obtained as a linear combination of the mean shape with these modes. The reconstruction of the original shape of the bone of interest is performed finding the best coefficients of this linear combination.

The difference between the segmented bone and the reconstructed bone is the erosion of which it is possible to calculate the volume and then the scoring. Processing takes a few minutes for all wrist bones (or hand bones), which leads to a substantial reduction of diagnosis time and costs.

3.4 RheumaSCORE in Clinical Applications

A preliminary clinical test has been carried out at DIMI[1]. 57 patients (42 women, median age 52 years, range 20-73 years, median disease duration 22 months, range 1-420 months) diagnosed with early RA according to the 1987 ACR criteria were studied. The wrists were imaged in an extremity-dedicated MRI device (Artoscan C, Esaote, Genova, Italy) using a turbo T1-weighted sequence. Some experts evaluated the erosion scores using the manual RAMRIS method and the RheumaSCORE software: perfect concordance was 45.2% at baseline, and 92.9% at follow up. Detailed informations can be found on the paper "An MRI study of bone erosions healing in the wrist and metacarpophalangeal joints of patients with Rheumatoid Arthritis".

Moreover, the framework permits the management and storage of clinical data (like C-reactive protein), useful for measurement and monitoring the disease activity of RA. Physicians can also add annotations, possibly using the system ontology, in order to highlight lessons learnt or critical issues linked to specific features of the current patient. All the information related to the patient's examination (e.g. acquired DICOM images, anatomical 3D segmented elements, 3D features, user annotations) are stored in the system database and are available for retrieval. The patient disease follow-up is supported by storing, visualizing and comparing several sets of data acquired at different times. Differences among parameters and trends can be computed and visualized.

References

1. Doi, K., Giger, M.L., MacMahon, H., et al.: Computer-aided diagnosis: development of automated schemes for quantitative analysis of radiographic images. Sem. Ultrasound CT MR **13**, 140–152 (1992)
2. Doi, K., Giger, M.L., Nishikawa, R.M., Hoffmann, K.R., MacMahon, H., Schmidt, R.A., et al.: Digital radiography: a useful clinical tool for computer-aided diagnosis by quantitative analysis of radiographic images. Acta. Radiol. **34**, 426–439 (1993)
3. Giger, M.L., Huo, Z., Kupinski, M.A., Vyborny, C.J.: Computer aided diagnosis in mammography. In: Fitzpatrick, J.M., Sonka, M. (eds.) The Handbook of Medical Imaging: Medical Imaging Processing and Analysis, vol. 2, pp. 915–1004. SPIE, Bellingham (2000)
4. Li, Q., Li, F., Armato III, S.G., Suzuki, K., Shiraishi, J., Abe, H., et al.: Computer-aided diagnosis in thoracic CT. Seminars in Ultrasound. CT MRI **26**, 357–363 (2005)

[1] *DIMI -Dipartimento di Medicina Interna, Clinica Reumatologica, Università degli Studi di Genova.*

5. Yoshida, H., Dachman, A.H.: Computer-aided diagnosis for CT colonography. Seminars in Ultrasound, CT MRI **25**, 404–410 (2004)
6. Moberg, K., Bjurstam, N., Wilczek, B., Rostgard, L., Egge, E., Muren, C.: Computer assisted detection of interval breast cancers. Eur. J. Radiol. **39**, 104–110 (2001)
7. Arimura, H., Katsuragawa, S., Suzuki, K., Li, F., Shiraishi, J., Doi, K.: Computerized scheme for automated detection of lung nodules in low-dose CT images for lung cancer screening. Acad. Radiol. **11**, 617–629 (2004)
8. Summers, R.M., et al.: Automated polyp detection at CT colonography: Feasibility assessment in the human population. Radiology **219**, 51–59 (2001)
9. White, P.M., Teasdale, E.M., Wardlaw, J.M., Easton, V.: Intracranial aneurysms: CT angiography andMRangiography for detection—prospective blinded comparison in a large patient cohort. Radiology **219**, 739–749 (2001)
10. Kubassova, O., Boesen, M., Cimmino, M.A., Bliddal, H.: A computer-aided detection system for rheumatoid arthritis MRI data interpretation and quantification of synovial activity. European Journal of Radiology **74**(3), 67–72 (2010)
11. RheumaSCORE. http://www.research.softeco.it/rheumascore.aspx
12. Barbieri, F., Parascandolo, P., Vosilla, L., Cesario, L., Viano, G., Cimmino, M.A.: Assessing MRI erosions in the rheumatoid wrist: a comparison between RAMRIS and a semiautomated segmentation software. Ann. Rheum. Dis. **71**(Suppl 3) (2012)
13. Sebastian, T.B., Tek, H., Crisco, J.J., Kimia, B.B.: Segmentation of carpal bones from CT images using skeletally coupled deformable models. Medical Image Analysis **7**(1), 21–45 (2003)
14. Duryea, J., Magalnick, M., Alli, S., Yao, L., Wilson, M., Goldbach-Mansky, R.: Semiautomated three-dimensional segmentation software to quantify carpal bone volume changes on wrist CT scans for arthritis assessment. Medical Physics **36** (2008)
15. Lodwick, G.S., Haun, C.L., Smith, W.E., et al.: Computer diagnosis of primary bone tumor. Radiology **80**, 273–275 (1963)
16. Myers, P.H., Nice, C.M., Becker, H.C., et al.: Automated computer analysis of radiographic images. Radiology **83**, 1029–1033 (1964)
17. Winsberg, F., Elkin, M., May, J., et al.: Detection of radiographic abnormalities in mammograms by means of optical scanning and computer analysis. Radiology **89**, 211–215 (1967)
18. Kruger, R.P., Towns, J.R., Hall, D.L., et al.: Automated radiographic diagnosis via feature extraction and classification of cardiac size and shape descriptors. IEEE Trans. Biomed. Eng. **19**, 174–186 (1972)
19. Kruger, R.P., Thompson, W.B., Turner, A.F.: Computer diagnosis of pneumoconiosis. IEEE Transactions on Systems, Man, and Cybernetics **4** (1974)
20. Toriwaki, J., Suenaga, Y., Negoro, T., et al.: Pattern recognition of chest x-ray images. Computer Graphics and Image Processing **2**, 252–271 (1973)
21. Engle, R.L.: Attempt to use computers as diagnostic aids in medical decision making: a thirty-year experience. Perspect. Biol. Med. **35**, 207–219 (1992)
22. Peloschek, P.L., Langs, G., Bischof, H., Kainberger, F., Kropatsch, W., Imhof, H.: Computer aided diagnosis (CAD) in rheumatoid arthritis : automated joint localization, estimation of the bone contour and consecutive detection of defects of the bone contour in metacarpal bones. In: Proceedings of the Annual Meeting of the Radiological Society of North America RSNA (2003)
23. Lorensen, W.E., Cline, H.E.: Marching cubes: a high resolution 3D surface construction algorithm. In: Proc. of ACM SIGGRAPH, pp. 163–169 (1987)

24. Markenson, J.A.: Worldwide trends in the socioeconomic impact and long-term prognosis of rheumatoid arthritis. Semin. Arthritis Rheum. **21**, 4–12 (1991)
25. Weinblatt, M.E.: Rheumatoid arthritis: treat now, not later [editorial]. Ann. Intern. Med. **124**, 773–774 (1996)
26. Østergaard, M., Hansen, M., Stoltenberg, M., Jensen, K.E., Szkudlarek, M., Pedersen-Zbinden, B., Lorenzen, I.: New radiographic bone erosions in the wrists of patients with rheumatoid arthritis are detectable with magnetic resonance imaging a median of two years earlier. Arthritis Rheum. **48**, 2128–2131 (2003)
27. Benton, N., Stewart, N., Crabbe, J., Robinson, E., Yeoman, S., McQueen, F.M.: MRI of the wrist in early rheumatoid arthritis can be used to predict functional outcome at 6 years. Ann. Rheum. Dis. **63**, 555–561 (2004)
28. McQueen, F.M., Benton, N., Perry, D., Crabbe, J., Robinson, E., Yeoman, S., McLean, L., Stewart, N.: Bone edema scored on magnetic resonance imaging scans of the dominant carpus at presentation predicts radiologic joint damage of the hands and feet six years later in patients with rheumatoid arthritis. Arthritis Rheum. **48**, 1814–1827 (2003)
29. Østergaard, M., Hansen, M., Stoltenberg, M., Jensen, K.E., Szkudlarek, M., Klarlund, M., Pedersen-Zbinden, M.: MRI bone erosions in radiographically non-eroded rheumatoid arthritis wrist joint bones give a 4-fold increased risk of radiographic erosions five years later. Arthritis Rheum. **46**(Suppl.), S526–S527 (2002)
30. Ejbjerg, B., McQueen, F., Lassere, M., Haavardsholm, E., Conaghan, P., O'Connor, P., Bird, P., Peterfy, C., Edmonds, J., Szkudlarek, M., Genant, H., Emery, P., Ostergaard, M.: The EULAR-OMERACT rheumatoid arthritis MRI reference image atlas: the wrist joint. Ann. Rheum. Dis. **64**(Suppl 1), 23–47 (2005)
31. Catalano, C.E., Robbiano, F., Parascandolo, P., Cesario, L., Vosilla, L., Barbieri, F., Spagnuolo, M., Viano, G., Cimmino, M.A.: Exploiting 3D part-based analysis, description and indexing to support medical applications. In: Greenspan, H., Müller, H., Syeda-Mahmood, T. (eds.) MCBR-CDS 2012. LNCS, vol. 7723, pp. 21–32. Springer, Heidelberg (2013)
32. Koch, M., Schwing, A.G., Comaniciu, D., Pollefeys, M.: Fully automatic segmentation of wrist bones for arthritis patients. In: Proceedings of the 8th IEEE International Symposium on Biomedical Imaging, from Nano to Macro, ISBI, Chicago, Illinois, USA, pp 636–640
33. Włodarczyk, J., Czaplicka, K., Tabor, Z., Wojciechowski, W., Urbanik, A.: Segmentation of bones in magnetic resonance images of the wrist. International Journal of Computer Assisted Radiology and Surgery **10**(4), 419–431 (2015)
34. Crowley, A.R., Dong, J., McHaffie, A., Clarke, A.W., Reeves, Q., Williams, M., et al.: Measuring bone erosion and oedema in rheumatoid arthritis: a comparison of manual segmentation and RAMRIS methods. J. Magn. Reson. Imaging **33**, 364–371 (2011)
35. Chand, A.S., McHaffie, A., Clarke, A.W., Reeves, Q., Tan, Y.M., Dalbeth, N., et al.: Quantifying synovitis in rheumatoid arthritis using computer-assisted manual segmentation with 3 Tesla MRI scanning. J. Magn. Reson. Imaging **33**, 1106–1113 (2011)
36. Parascandolo, P., Cesario, L.,Vosilla, L., Pitikakis, M., Viano, G.: Smart brush: a real time segmentation tool for 3D medical images. In: 8th International Symposium on Presented at Image and Signal Processing and Analysis (ISPA), pp. 689–694 (2013)
37. Caselles, V., Kimmel, R., Sapiro, G.: Geodesic active contours. In: International Conference on Computer Vision, pp. 694–699. IEEE Computer Society Press (1995)