http://jmscr.igmpublication.org/home/
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v8i4.92

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Research Article

HRCT Chest Findings in Patients with Rheumatoid Arthritis Associated - Interstitial Lung Disease (RA-ILD)

Authors
Areca Wangnoo[1], Pankaj Banotra[1], Mohit Sharma[1], Annil Mahajan[2]
[1]Residents, Department of General Medicine, Government Medical College, Jammu
[2]Professor & HOD, Department of General Medicine, Government Medical College, Jammu
*Corresponding Author
Areca Wangnoo

Abstract
Rheumatoid arthritis is a chronic inflammatory systemic disease with a number of extra- articular manifestations including lung disease. Our purpose of the study was to assess the HRCT findings in patients with rheumatoid arthritis associated lung diseases (RA-ILD).
Materials and Methods: *A cross sectional study was conducted ona total of 36 patients of Rheumatoid arthritis associated interstitial lung disease (RA-ILD). Patients were evaluated by physiological (pulmonary function test) and radiological methods (chest X-ray, HRCT chest). Chi-square test was used for comparison of categorical variables. A p value of less than 0.05 was considered statistically significant*
Results: *UIP was the most common ILD seen in RA in our study. Chest X Ray showed reticulonodular pattern in 39.3% of patients, prominent vascular makings in 7.1% of patients and bilateral lower zone haziness in 32.1% of patients. PFT with restrictive pattern was seen in 50% of patients and obstructive pattern was seen in 7.1% of patients. On HRCT, reticulations were present in 35.7% of patients: honey combing was present in 53.6% of patients, ground glass opacities in 42.9%, pleural thickening in 10.7%, pleural effusion in 7.1%, pulmonary vascular prominence in 7.1%, rheumatoid nodules in 7.1% and bronchiectasis in 7.1%.*
Conclusion: *In the present study, UIP is the most common ILD. Honey combing and ground glass opacities most common finding on HRCT in these patients. As the duration of illness increases, need for screening for pulmonary involvement with Chest Xray, PFTs and HRCT is to be emphasized along with periodic chest examination.*
Keywords: *Pulmonary, Rheumatoid Arthritis, Interstitial lung diseases, RA-ILD.*

Introduction

Rheumatoid arthritis affects ~1% of the population in developed countries. The incidence and prevalence of rheumatoid arthritis in developing countries is thought to be lower, but is difficult to quantify.[1,2] Although joint disease is the main presentation, there are a number of extra-articular manifestations including subcutaneous nodule formation, vasculitis, inflammatory eye disease and lung disease.[3,4] Of these manifestations, lung disease is a major contributor to morbidity and mortality.

ILD is the most common pulmonary manifestation of rheumatoid arthritis lung disease.[5] Most of these patients have changes consistent with ILD on either chest radiograph, High-resolution computed tomography (HRCT), pulmonary function testing (PFT), bronchoalveolar lavage (BAL).Of these patients, 76% had clinically silent disease.[6] It is currently estimated that ∼30% of patients with rheumatoid arthritis have subclinical ILD noted on HRCT scans. [5]

Epidemiology/Risk Factors

Although rheumatoid arthritis is more common in females, rheumatoid arthritis associated-ILD (RA-ILD) occurs more frequently in males, with a male to female ratio as high as 2:1 in some studies. [7,8] Onset of lung disease typically occurs in the fifth to sixth decade of life. [9] Age has consistently been shown to be a risk factor for the development of ILD. [10] Another major risk factor is a history of smoking, with one study finding an odds ratio of 3.8 for those who smoked >25 pack-years. [11] High levels of rheumatoid factor are a known risk factor involving formation of circulating immune complexes.[12]

Pathogenesis

The mechanism of pulmonary fibrosis occurring in ILD is not well understood. Patients with rheumatoid arthritis typically have circulating autoantibodies, the most common being rheumatoid factor and anti-cyclic citrullinated peptide (CCP). [13] Anti-CCP antibodies have also been associated with the development of airway disease. [14]

Cigarette smoking may play a role in inducing antibody formation and has been linked to higher titres of rheumatoid factor. [11] Smoking may promote citrullination of lung proteins, thus leading to the development of anti-CCP antibodies.

Pulmonary Function Tests

The majority of patients with RA-ILD will have a restrictive pattern on PFTs, with or without decreased diffusing capacity of the lung for carbon monoxide (DLCO) and hypoxemia. [7] Airflow obstruction may coexist and be seen in patients manifesting airway involvement, i.e. bronchiolitis obliterans.

Imaging

In UIP, HRCT scans show subpleural, basal predominant, reticular abnormalities with honeycombing, and traction bronchiectasis but a relative absence of ground-glass opacities.[15] NSIP is the second most common pattern, occurring in ∼11–32% of patients. NSIP is characterised by basilar predominant ground-glass opacities and absence of honeycombing. Additional patterns less commonly seen in rheumatoid arthritis include other patterns of interstitial pneumonia, including organising pneumonia, diffuse alveolar damage (DAD), lymphocytic interstitial pneumonia (LIP) and desquamative interstitial pneumonia (DIP)-like patterns. [16]

Prognosis

ILD is second only to cardiac disease as a cause of mortality in rheumatoid arthritis [7,8] The mean survival for RA-ILD overall has been estimated at 2.6 years from time of diagnosis compared to 9.9 years for rheumatoid arthritis patients without lung involvement; however, this probably reflects the predominance of the UIP pattern.[9]

Methodology

A cross sectional study conducted in a tertiary centre after obtaining ethical clearance during a period of 1 year from Nov 2017 to Nov 2018. A total of 36 patients of Rheumatoid arthritis associated lung diseases of either sex having age >21 years who met the ACR EULAR (2010) criteria for RA were included.[1]Patients with history of cardiopulmonary disorder, collagen vascular disease (SLE, scleroderma) ,viral infection (hepatitis B & C, HIV), tuberculosis and inhalational exposure / occupational lung disease (asbestos, silica) were excluded.

Patients were examined clinically for respiratory signs and symptoms. Patients were further evaluated for pulmonary manifestations by physiological (pulmonary function test) and radiological methods (chest X-ray, HRCT chest).

In patients with clinical suspicion of tuberculosis sputum for AFB was done for exclusion of pulmonary tuberculosis. Patients with evidence of pulmonary fibrosis on HRCT chest were further investigated for HBsAg, anti-HCV, HIV to rule out pulmonary fibrosis secondary to viral infections. Majority of our patients were on DMARDs and were not excluded from our study.

Statistical Analysis

Continuous variables were expressed as Mean±SD and categorical variables were summarized as percentages. Chi-square test was used for comparison of categorical variables. Graphically the data was presented by bar and pie diagrams. A p value of less than 0.05 was considered statistically significant.

Results

Age distribution of RA-ILD patients shows that 7.1% of patients were in 31-40 years of age group, 25% of patients were in 41-50 years of age group, 39.3% of patients were in51-60 years of age group and 28.6% of patients were in > 60 years of age. (Figure 1)

Chest X Ray was normal in 28.6% of patients, reticulonodular pattern in 39.3% of patients, prominent vascular makings in 7.1% of patients and bilateral lower zone haziness in 32.1% of patients. (Table 1)

PFT was normal in 28.6% of patients, restrictive pattern was seen in 50% of patients, obstructive pattern was seen in 7.1% of patients and 14.3% of patients were not cooperative for PFT. (Figure 2)

As per HRCT Pattern. Reticulations were present in 35.7% of patients: honey combing was present in 53.6% of patients, ground glass opacities in 42.9%, pleural thickening in 10.7%, pleural effusion in 7.1%, pulmonary vascular prominence in 7.1%, rheumatoid nodules in 7.1% and bronchiectasis in 7.1%.(Figure 3)

Among the patients with RA-ILD, 72.73% of males had UIP while 47.06% of females had UIP and 27.27% of males had NSIP while 52.94% of females had NSIP. (Figure 4)

Figure 1 Age Distribution of RA-ILD Patients

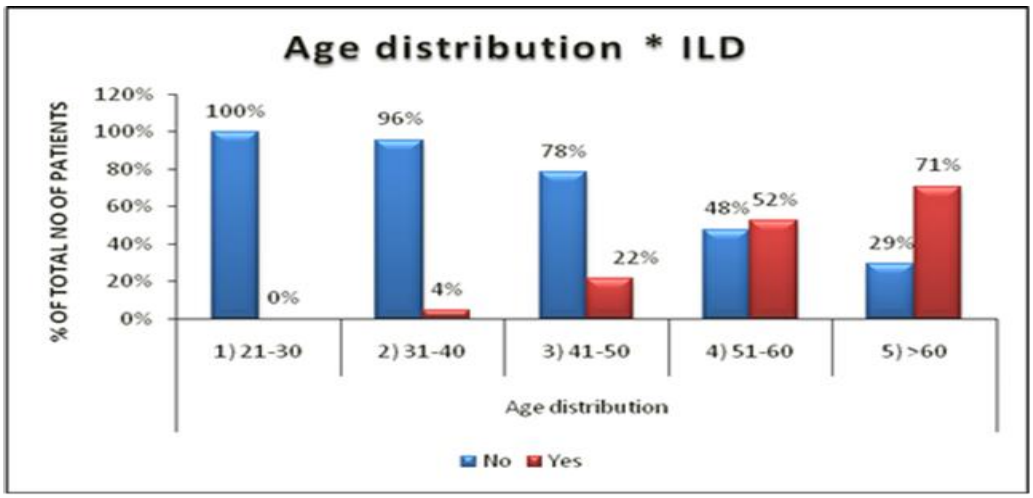


Table 1: Distribution of RA-ILD patients as per chest X-Ray findings

Chest X-Ray Findings	No. of patients	Percentage
Normal	8	28.6%
Reticulonodular Pattern	11	39.3%
Prominent Vascular Markings	2	7.1%
Bilateral Lower zone Haziness	9	32.1%

Figure 2: Distribution of RA-ILD patients as per PFT findings

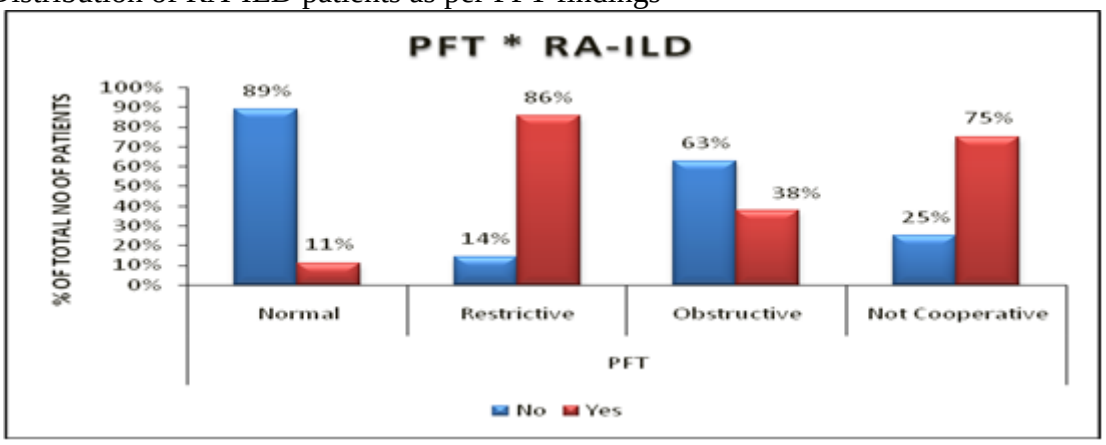


Figure 3: Distribution of RA-ILD patients as per HRCT findings

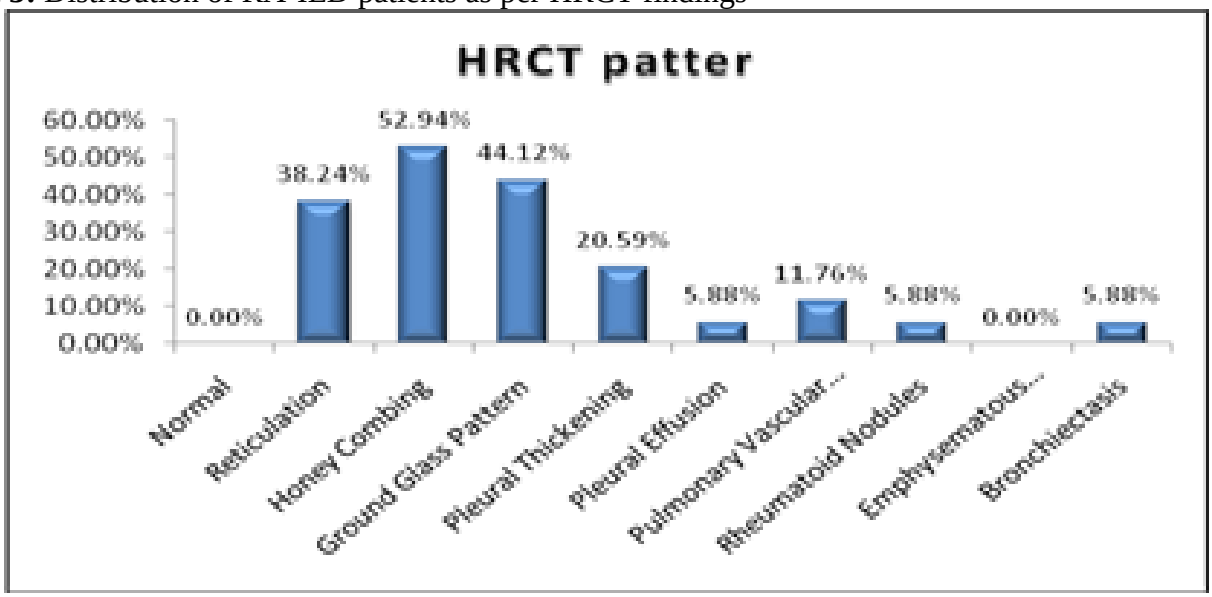
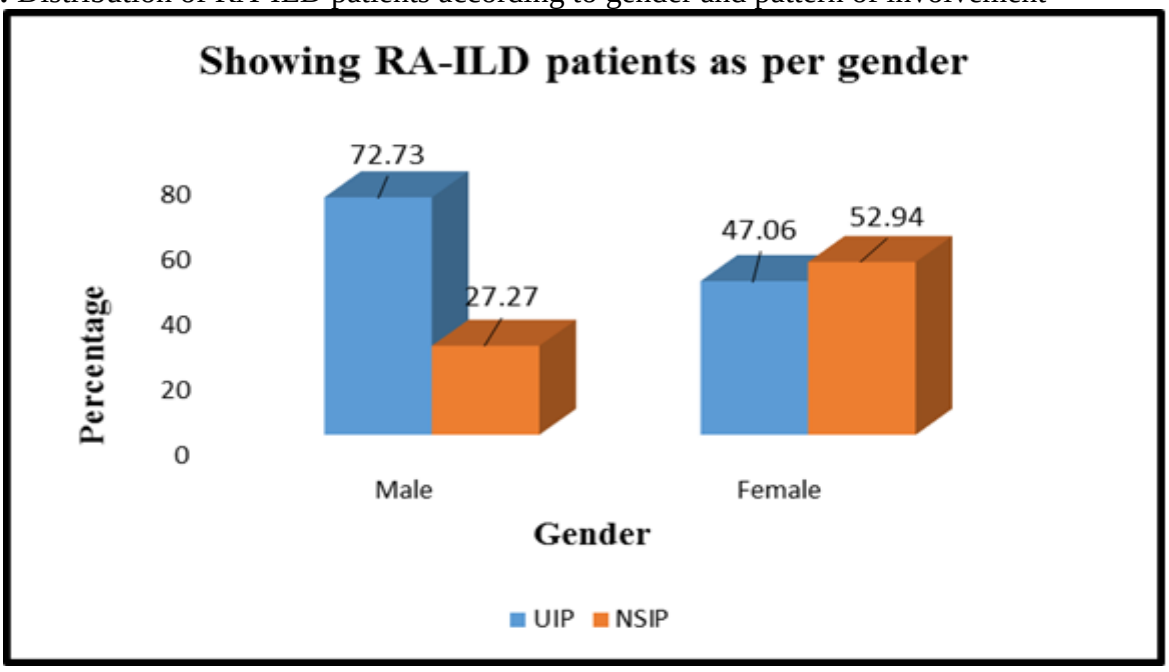


Figure 4: Distribution of RA-ILD patients according to gender and pattern of involvement



Discussion

Rheumatoid arthritis (RA) is an autoimmune disease affecting 0.5-1% of the world population. Being a multisystem disorder, RA virtually affects every organ system of the body and one of the major causes of mortality in patients of RA is lung involvement, cardiovascular involvement being most important cause.

The percentage of patients with lung involvement in age group > 60 years dropped to 28.6% as compared to 39.3% in age of 51-60 years. The lesser proportion of patients in age more than 60 years can be attributed to higher mortality of RA in this age group, but further studies are needed to validate our assumption. The results in our study were in comparison with the study conducted by Kelly et al**.** (2014)who demonstrated that median age at diagnosis of RA was 56 years (range 23-76).[13] Similarly Assayag D et al. (2014), studies mean age ranged 55 to 69 years in RA-ILD.[10] Our findings were also consistent with study done by Bilgici A et al. (2005). [17]

Chest X ray being the primary imaging modality for screening of lung pathology revealed abnormality in about three quarters of patients with reticulonodular pattern and lower lobe haziness in 39.3% and 32.1% of patients respectively. Similar findings were as demonstrated by N. Fatima et al. (2013) who found that the predominant finding on chest X-ray was reticulonodular pattern.[18]

Sixteen (57.1%) patients had UIP with reticulation with or without honeycombing on HRCT and 12 (42.9%) patients had NSIP with predominant ground glass opacities on HRCT. UIP was the most common ILD seen in RA in our study. In the study done by DeLauretis et al (2011), NSIP was the most common pattern in all CTDs, except for RA which is characterized by a higher frequency of UIP.[8] Similarly, Kelly et al (2014) also studied that UIP was the most common subtype on HRCT.[13] UIP was predominantly seen in 65% followed by NSIP in 24%. In our study, second most common pattern was NSIP; Similar results were seen by Lee HK et al. (2005)[21] UIP was more common in males compared to NSIP as reported by similar studies.[18-21]

Pulmonary function test was abnormal in 16 (57.1%) patients with predominant restrictive pattern in 14 (50%) patients. In the study done by N. Fatima et al. (2013), 27 patients (43%) had abnormal PFT with restrictive pattern in 18 (29%) and obstructive pattern in 5 (8%) of patients. [18] In similar studies, restrictive pattern was seen in 52.9% and obstructive pattern in 11.8% of patients.[22,23]

Stressing upon the fact, that, early recognition and treatment of RA-ILD can halt or modify lung involvement in RA. These findings on the imaging modalities and physiological testing can be used for the early diagnosis of the entity.

Conclusion

In the present study, UIP is the most common ILD. Honey combing and ground glass opacities most common finding on HRCT in these patients. As the duration of illness increases, need for screening for pulmonary involvement with Chest X ray, PFTs and HRCT is to be emphasized along with periodic chest examination.

References

1 **Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO *et al.*** Rheumatoid arthritis classification criteria: an American College of Rheumatology / European League Against Rheumatism collaborative initiative. *Ann Rheum Dis* 2010; 69: 1580-8

2 **Richman N, Yazdany J, Graf J, Chernitskiy V, and Imboden J.**Extra-articular manifestations of rheumatoid arthritis in a multiethnic cohort of predominantly Hispanic and Asian patients. *Medicine* 2013; 92: 92-7

3 **Hamblin M. and Horton M.** Rheumatoid arthritis-associated interstitial lung disease: diagnostic dilemma. *Pulmon Med* 2011: 1-12

4 **Chan E, Chapman K. and Kelly C.** interstitial lung disease in rheumatoid arthritis; a review. *Arthritis Research Topical Reviews Series* 2013; 7: 1-4.

5 **Doyle TJ, Lee JS, Dellaripa PF, Lederer JA, Matteson EL, Fischer A, *et al.*** A roadmap to promote clinical and translational research in rheumatoid arthritis-associated interstitial lung disease. *Chest* 2014; 145: 454-63

6 **Gabbay L, Tarala R, Will R, Carroll G, Adler B, Cameron D. *et al.*** Interstitial limy disease in new onset rheumatoid arthritis. *American Journal of Respiratory and Critical Care Medicine* 1997; 156(2 (Part 1)): 528-36

7 **Cavagna L, Monti S, Grosso V, Boffini N,Scorletti E**, **CrepaldiG , et al.** The multifaceted aspects of interstitial lung disease in rheumatoid arthritis. Biomed Res Int 2013; 2013: 759-60

8 **De Lauretis A, Veeraraghavan S, Renzoni E.** Connective tissue disease-associated interstitial lung disease: how does it differ from IPF? How should the clinical approach differ? Chron Respir Dis 2011; 8:53-82

9 **Bongartz T, Nannini C, Medina-Velasquez YF, Achenbach SJ, Crowson CS, Ryu JH et al.** Incidence and mortality of interstitial lung disease in rheumatoid arthritis: a population-based study. *Arthritis Rheum* 2010 Jun;62: 1583-91

10 **Assayag D, Lubin M, Lee JS, King TE, Collard HR, Ryerson CJ.** Predictors of mortality in rheumatoid arthritis-related interstitial lung disease. *Respirology* 2014; 19: 493-500

11 **Saag KG, Cerhan JR, Kolluri S, Ohashi K, Hunninghake GW, Schwartz DA.** Cigarette smoking and rheumatoid arthritis severity. *Ann Rheum Dis* 1997; 56: 463-9

12 **Turesson C, Jacobsson L, Sturfelt G, Matteson E, Mathsson L. and Ronnelid J. *et al.*** Rheumatoid factor and antibodies to cyclic citrullinated peptides are associated with severe extra-articular manifestations in rheumatoid Arthritis. *Ann Rheum Dis* 2007; 66: 59-64

13 **Kelly C, Saravanan V, Nisar M, Arthanari S, Woodhead F, Price-Forbes A, Dawson J, *et al.*** Rheumatoid arthritis-related interstitial lung disease: associations, prognostic factors and physiological and radiological characteristics – a large multicentre UK study. *Rheumatology* 2014; 53: 1676-82

14 **Fischer A, Solomon JJ, du Bois RM, Deane KD, Olson AL, Fernandez- Perez ER, *et al.*** Lung disease with anti-CCP antibodies but not rheumatoid arthritis or connective tissue disease *Respir Mod* 2012; 106: 1040-7

15 **Raghu G, Collard HR, Egan JJ, Martinez FJ, Behr J, Brown KK, *et al.*** An official ATS/ ERS/ JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. *Am J Respir CritCare Med* 2011; 183: 788-824

16 **Cottin V, Cordier JF.** Combined pulmonary fibrosis and emphysema in connective tissue disease. *CurrOpinPulm Med* 2012; 18:418-27

17 **Bilgici A, Ulusoy H, Kuru O, Celenk C, Unsal M, Danaci M *et al.*** Pulmonary involvement in rheumatoid arthritis. *Rheumatol Int* 2005; 25: 429-35

18 **Fatima N, Shameem M, Malik A, Khan PA, Shujatullah F, Ahmed S, Nabeela**. A Study on the Pulmonary Manifestations of Rheumatoid Arthritis from a North Indian Town. *Open Journal of Respiratory Diseases*.2013; 3: 128-31

19 **Kim EJ, Collard HR and King TE.** Rheumatoid Arthritis-Associated Interstitial Lung Disease: The Relevance of Histopathologic and Radiographic Pattern. *Chest* 2009; 136: 1397-1405

20 **Dawson J, Fewins H, Desmond J, Lynch M and Graham D.**Predictors of progression of HRCT diagnosed fibrosing alveolitis in patients with rheumatoid arthritis. *Ann Rheum Dis* 2002; 61: 517-21

21 **Lee HK, Kim DS, Yoo B, Seo JB, Rho JY, Colby TV, Kitaichi M.** Histopathologic pattern and clinical features of rheumatoid arthritis-associated interstitial lung disease. *Chest* 2005; 127: 2019-27

22 **Balbir-Gurman A, Yigla M, Nahir AM, Braun-Moscovici Y.** Rheumatoid pleural effusion. *Semin Arthritis Rheum.*2006; 35:368–378

23 **Biederer J, Schnabel A, Muhle C, Gross W, Heller M, Reuter M. *et al.*** Correlation between HRCT findings, pulmonary function tests and bronchoalveolar lavage cytology in interstitial lung disease associated with rheumatoid arthritis. *Eur Radiol* 2004; 14: 272-80.