We read with interest the paper by Carotti et al 1 that appeared in the October issue of the Annals of the Rheumatic Diseases. 2 The authors investigated the usefulness of contrast enhanced power Doppler ultrasonography (PDS) in determining the vascularisation rate of the synovial pannus of patients with rheumatoid arthritis (RA). After intravenous infusion of an echo contrast (Levovist, Schering, Germany) PDS was performed on the knee joints of 42 patients with RA, who had previously been classified as having active (n=15), moderately active (n=14), and inactive knee synovitis (n=13). The results were expressed as the area underlying time-intensity curves. Highest vascularisation scores were found in patients with active synovitis (216.2 (33.4), mean (SD)), whereas lower values were found in those with moderately active (186.8 (25.8)) and inactive synovitis (169.6 (20.6)). Significant difference (p<0.01) was found between the active and the inactive group only. Also, significant correlations were found between the vascularisation scores and some indices of the disease activity. The authors concluded that PDS may be a valuable method of distinguishing between inflammatory and non-inflammatory pannus of knee joints in RA and thus may have a clinical potential for both diagnostic and therapeutic purposes.

Unfortunately, Carotti et al did not provide any data on the sensitivity and specificity of the method used. Moreover, no figure showing distribution of the vascularisation scores in individual patients and/or confidence limits of the mean was available. This is a major problem and, in our opinion, the data presentation does not allow for any conclusions about how the PDS really performs in clinical settings. It should be emphasised that statistical significance alone is not sufficient as it could easily be achieved if there were some lower and some higher vascularisation scores in patients with inactive and active synovitis, respectively.

We are aware that the study was designed as a preliminary one and a relatively small group of patients was included. Nevertheless, we believe that all Annals readers would benefit much from seeing the sensitivity and specificity figures/estimates or the presentation of the individual vascularisation scores. We wonder if these could be provided by the authors.

The statement that ultrasonography offers a simple, non-invasive, reproducible, non-radiating, and inexpensive imaging technique was made several times in the paper. It holds true for ultrasonography as a general imaging technique. However, it seems somewhat misleading in the context of the methodology used by the authors. PDS is not a simple technique as it requires a team of well trained and experienced radiologists and technicians who are aware of possible caveats of the method. The procedure requires venepuncture and an intravenous contrast infusion, and thus can at most be regarded as a low invasive one. It should be emphasised that Levovist, although generally well tolerated, may rarely lead to some adverse reactions (for example, local tissue irritations, dyspnoea, changes in pulse/blood pressure, nausea, vomiting, headaches, dizziness, skin reactions—data taken from the compound data sheet). To our knowledge, no data exist on the reproducibility of PDS for the knee pannus examination. A high-end equipment has to be used to achieve good results which is relatively expensive. It seems that from the long list of adjectives used by the authors, “non-radiating” is the only valid one for the PDS method described.

With regard to the sensitivity and specificity of the PDS technique, as far as we know no data have been reported. Our study has all the features of a preliminary investigation and, obviously, cannot answer all the questions on the topic. However, the receiver operating characteristic (ROC) curve was employed to describe how well various values of the area underlying the enhancement curves of the PDS can detect patients with RA with high and low synovitis activity (fig 1). This analysis involves plotting the true positive rate (sensitivity) against the false positive rate (100 − specificity) for possible cut off scores. Sensitivity and specificity (which constitute the discriminating ability of a test) were used in agreement with the current definitions of these terms. 3 Moreover, we calculated 95% confidence intervals (CI) of sensitivity and specificity. Each point on the ROC plot represents a sensitivity/specificity pair corresponding to a particular decision threshold. 4 The area under the ROC curve is used to evaluate the screening scale's performance. For PDS, the mean area under the curve is 0.859 (0.072); 95% CI 0.675 to 0.960. According to Swets et al, areas from 0.50 to about 0.70 represent poor accuracy, those from 0.70 to 0.90 are “useful for some purposes”, and higher values represent high accuracy. 5 From the ROC curve in fig 1 we computed the optimal cut off point, corresponding to the maximum sum of sensitivity and specificity. For our method an optimal point of 191 comes close to maximising both sensitivity and specificity. With this cut off point for the area under the time-intensity curve, the sensitivity is 80.0% and specificity is 84.6%. These findings have implications for both clinical practice and research purposes in assessment of disease activity in patients with RA.

Figure 2 shows the distribution of PDS scores in individual patients with active and non-active synovitis and the corresponding confidence limits of the mean. The mean (SD) values of the areas under the curves showed a significant difference (p<0.01) between the patients with active synovitis (216.2 (33.4); 95% CI 193.1 to 239.4) and those with inactive synovitis (169.6 (20.6); 95% CI 148.8 to 179.4).

Authors’ reply
We thank Drs Hrycaj and Lacki very much for their comments because we give the opportunity to illustrate further details of our study. Recent papers have shown a very close relationship between the results of power Doppler sonography (PDS) and those of dynamic gadolinium (Gd) enhanced magnetic resonance imaging (MRI) of the knee joint in patients with RA. 6 This study confirms that contrast enhanced PDS significantly improves the detection of intra-articular vascularity, compared with the unenhanced technique. 7 Contrast enhanced PDS demonstrated significant difference in intra-articular colour flow signals between joints of patients with inactive RA and those with active RA, between joints of patients with inactive RA and those with moderately active RA, and between joints of patients with moderately active RA and those with active RA.

Figure 1 shows the ROC curve illustrating the relation between sensitivity and complement of specificity (100−specificity) in rheumatoid patients for the PDS, with the index of synovitis activity as the external criterion (inactive synovitis v active synovitis). The triangle on the curve shows the optimal cut off point, corresponding to the highest sensitivity/specificity combination.
A case of orbital myositis associated with rheumatoid arthritis

In the October 2002 issue of the *Annals of Rheumatology and Associated Diseases* (OM) described a case of orbital myositis (OM) associated with rheumatoid arthritis (RA) and suggested that the major differential diagnosis was thyroid ophthalmopathy.1 The mechanical component of orbital involvement in Graves’ disease (GD) can produce diplopia (5–10%), proptosis, chemosis, scleral injection, and retrobulbar pressure or pain, whereas eyelid lag or retraction and stare are caused by the spastic component (in some cases lid retraction can be obscured by periocular edema). The extraocular muscles most commonly affected are the medial and inferior rectus muscles.

The authors suggested characteristics which would distinguish the two conditions, and among these they included the systemic manifestations of GD. GD should be seen as a systemic disease with various combinations of hyperthyroidism, ophthalmopathy, and dermopathy. Current pathogenetic theory shows that ophthalmopathy itself is a direct, independent manifestation of autoimmune; caused by autoimmunity to the thyrotropin receptor expressed by the preadipocyte subpopulation of orbital fibroblasts, mediated by type 2 helper T cells and thyroid stimulating antibodies. Moreover, it is well established that ophthalmopathy may precede hyperthyroidism or occur after its resolution (particularly in smokers after treatment with radioactive iodine). GD can be found in association with other autoimmune disorders such as type 1 diabetes mellitus, Addison’s disease, vitiligo, pernicious anemia, alopecia areata, myositis, systemic lupus erythematosus, Sjögren’s syndrome, and other HLA-D3 associated diseases. The association with rheumatoid arthritis is rarer, but recognised, even in multiple autoimmune syndromes. So where there is a commonality with involvement the absence of clinical hyperthyroidism should not rule out the diagnosis of GD.

Finally, the diagnosis of thyroid ophthalmopathy was unlikely because only one eye was affected. As suggested by the authors, magnetic resonance imaging is indicated to establish the correct diagnosis. This would show oedematous extraocular muscles with enlargement of the tendons in OM, and normal tendons in GD. Early response to systemic glucocorticoids confirms the diagnosis of OM.

Another disease that should be considered in the differential diagnosis is arteriovenous malformation, such as indirect carotid-cavernous fistula, which can develop spontaneously in older women. In this case the presence of a diffuse head murmur would be an important observation.2

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References

Authors’ reply
We thank Dr Fadini for his interest in our case report of orbital myositis in association with rheumatoid arthritis.1 He rightly discusses in some detail the possibility of thyroid ophthalmopathy occurring in the absence of a systemic hyperthyroid diathesis. As we made clear in our article, there is a considerable variety of presenting clinical features in this condition. We sought to present these as concisely as possible, with particular reference to the most common presentation.

The differential diagnosis of an arteriovenous malformation was not likely in the clinical setting outlined. We agree that, ultimately, the diagnosis was made on the...
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- Nightmare on Lambeth Palace Road

Further details: Dr Graham R V Hughes, Lupus Research Unit, The Rayne Institute, St Thomas’ Hospital, London, SE1 7EH. Tel: 020 7928 9292 ext. 2888/3357. Fax: 020 7633 9422. Email: sandy.hampson@kcl.ac.uk

NOTICES
MSc Programme in Clinical Rheumatology
Applications are invited for places on this MSc programme, starting September 2003, which provides an excellent academic basis for those aiming at a career in rheumatology or a related subject. Applicants should be medically qualified and should have had at least two years of general medical experience after qualification. Previous experience in rheumatology is desirable, but not essential. The programme is undertaken part time over two years and is now well established, entering its ninth year.

Topics covered will include: basic science, clinical skills, peripheral joint problems, spinal problems, connective tissue disease and vasculitis, and the epidemiology of musculoskeletal diseases. A supervised project, which may be either clinical or laboratory based, is an integral part of the programme. The closing date for applications is 30 May 2003.

Further details can be obtained from Miss Lisa McClair, ARC Epidemiology Unit, Stopford Building, University of Manchester, Oxford Road, Manchester, M13 9PT, UK. Tel: (0) 161 275 5993. Fax: (0) 161 275 5043. Email: Lisa.Mcclair@man.ac.uk

Ten topics in rheumatology
A two day postgraduate course in advanced rheumatology will be held at St Thomas’ Hospital, London on 5 and 6 June 2003. The registration fee is £120, and 60 subsidised registrations are offered at £20 to current SpRs to the first 60 applications received. CME accreditation is an integral part of the programme. The topics may be either clinical or laboratory based, is an integral part of the programme. The closing date for applications is 30 May 2003.

Further details can be obtained from Miss Lisa McClair, ARC Epidemiology Unit, Stopford Building, University of Manchester, Oxford Road, Manchester, M13 9PT, UK. Tel: (0) 161 275 5993. Fax: (0) 161 275 5043. Email: Lisa.Mcclair@man.ac.uk

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- What's new in RA?
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30th Annual Meeting of the International Society for the Study of the Lumbar Spine
13–17 May; Vancouver, Canada
Contact: Dr S Boden, Sunnybrook and Women's Health Science Center, Room MG 323, 2075 Bayview Avenue, Toronto, Canada M4N 3M5
Tel: 416 480 4833
Fax: 416 480 6055
Email: shirley.fitzgerald@swchsc.on.ca

4th European Congress of Rheumatology
18–21 June 2003; Lisbon, Portugal
Contact: Fred Wyss, Executive Secretary EULAR, Wilikonstrasse 15, CH-8032, Zurich, Switzerland
Tel: +41 1 383 9690
Fax: +41 1 383 9810
Email: eular@bluewin.ch
Website: www.eular.org

25th Annual Meeting of the American Society for Bone and Mineral Research (ASBMR)
19–23 September 2003; Minneapolis, Minnesota, USA
Tel: +1 202 367 1161
Fax: +1 202 367 2161
Email: asbmr@dc.sba.com
Website: www.asbmr.org

7th EULAR Sonography Course
9–12 October, 2003; Rome, Italy
An introductory and practical course on musculoskeletal ultrasonography
Scientific secretariat: Professor Guido Valesini
Email: annamaria.iagrocco@uniroma1.it
Contact: Organising secretariat: Michela Civelli, EDRA Spa, Medical Publishing and News Media, Viale Monza, 133 - 20125, Milan, Italy
Tel: +39 (0)2 281 72300
Fax: +39 (0)2 281 72399
Email: edracongressi@dsmedigroup.com

OARSI World Congress on Osteoarthritis
12–15 October 2003; Berlin, Germany
Tel: +1 856 439 1385
Fax: +1 856 439 0525
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Website: www.oarsoi.org

Fourth International Symposium on Clinical and Economic Aspects of Osteoporosis and Osteoarthritis
14–17 November 2003; Nice, France
Contact: Organisation Secretariat, YP Communication, 108 boulevard G Kleyer, 4000 Liège, Belgium
Tel: +32 (4) 254 12 25
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Email: yoland@piettecommunication.com
Website: http://nice.piettecommunication.com

XIIth International Conference on Behçet’s Disease
24–27 October 2004; Antalya, Turkey
Contact: Congress Secretariat, Figur Congress and Organization Services Ltd. STL Ayazmadesi Cad. Karadut Sok. No: 7 80088 Dikilitas, Istanbul
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Website: www.behcet2004.org

Future EULAR congresses
9–12 June 2004; EULAR 2004; Berlin, Germany
8–11 June 2005; EULAR 2005; Vienna, Austria
21–24 June 2006; EULAR 2006; Amsterdam, The Netherlands

Future ACR meetings
24–28 October 2003; 67th Annual Scientific Meeting; Orlando, Florida
16–21 October 2004; 68th Annual Scientific Meeting; San Antonio, Texas

Reference
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