Clinical usefulness of high resolution computed tomography in cryptogenic fibrosing alveolitis

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Despite recent technological advances, agreement amongst clinicians on an algorithm for the optimal management of cryptogenic fibrosing alveolitis (CFA) has proved to be elusive. The non-invasive diagnosis of CFA is often uncertain as the clinical features may mimic those of other interstitial lung diseases. Even when the diagnosis is secure, therapeutic decisions are not straightforward. Reversible inflammatory disease requires aggressive treatment, but side effects from an over-vigorous approach to irreversible fibrotic disease need to be avoided. The extent of disease may influence the approach to treatment, but the optimal means of staging initial severity remains contentious. Furthermore, precision in monitoring changes in disease severity at follow up is unattainable in some cases and this complicates therapeutic decisions. This review explores the impact of high resolution computed tomographic (CT) scanning on the diagnosis and management of CFA.

The integration of a new test into routine management is the product of rigorous initial assessment and subsequent accumulated clinical experience. Enduring changes in clinical practice seldom result solely from “landmark” series. For example, early reports suggested that bronchoalveolar lavage (BAL) might offer invaluable additional diagnostic and prognostic information in diffuse lung disease. However, subsequent clinical experience has shown that diagnostic and prognostic trends obtained from BAL in groups of patients are not sufficiently robust to change management substantially in most cases. In the same way, although disease activity defined by 67-gallium scanning was shown to correlate with inflammatory cell content on open lung biopsy material, it transpired that 67-gallium scanning did not predict responsiveness to treatment. Initial enthusiasm generated by early studies of diagnostic tests followed by disappointment is a familiar cycle for clinicians managing patients with interstitial lung disease.

Will this sequence of events apply equally to the use of CT scanning in the management of CFA? Crucially, the role of CT scanning in routine management is now validated by a decade of clinical experience and extended by technological advances. The optimal CT protocol for the evaluation of diffuse lung disease (high resolution CT scanning) was developed in the late 1980s. Important modifications included the high spatial frequency (or “bone”) reconstruction algorithm which sharpens image definition substantially by reducing image smoothing at the cost of an apparent increase in noise, and a second equally important development—reduced section thickness. It is now accepted that the best visualisation of fine detail is achieved with 1–2 mm collimation; with collimation of less than 1 mm, signal noise outweighs the benefits of fine morphological depiction. One important advantage of high resolution CT scanning is the decrease in radiation burden compared with conventional continuous section CT scanning. A standard high resolution protocol of 1.5 mm sections at 20 mm intervals from the lung apices to the bases carries a radiation dosage equivalent to 6–8 chest radiographs. Lower dose protocols may provide roughly comparable information to standard protocols in most patients but have yet to be validated clinically. Standard high resolution CT protocols have now been in place throughout the 1990s in most tertiary centres.

Before the advent of CT scanning the non-invasive diagnosis of CFA was often insecure. Clinical diagnostic criteria (bilateral crackles, chest radiographic abnormalities compatible with bilateral fibrosis, lack of significant exposure to agents known to induce lung fibrosis and, in some series, a restrictive defect or isolated fall in gas transfer) were necessarily non-specific and this led some clinicians to advocate routine early open lung biopsy in patients with suspected CFA. However, others questioned whether the clinical benefit conferred by diagnostic certainty justified thoracotomy; except in tertiary institutions, the median age of patients presenting with CFA in the UK was in the seventh decade. Thus, even before CT scanning, fewer than 10% of patients with CFA in the UK had open lung biopsies in the late 1980s and early 1990s compared with 50% at one tertiary institution.

The precise impact of CT scanning on the non-invasive diagnosis of CFA cannot be deduced solely from the major radiological diagnostic studies of the late 1980s and early 1990s. The diagnostic sensitivity of CT scanning was evaluated in five series on a total of 501 patients with interstitial lung disease (excluding one study using inexperienced observers); in 145 patients in these five studies with a final diagnosis of fibrosing alveolitis, a correct first choice diagnosis was made in 84% on CT scanning compared with 73% on chest radiography. There are difficulties in attempting meta-analysis of these series as CT protocols (including collimation thickness) and patient characteristics differ between institutions. However, the results are remarkably similar and, on the face of it, suggest that CT scanning enjoys a definite but inconclusive diagnostic advantage over chest radiography. It is probable that the impact of CT scanning on
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The diagnostic power of CT scanning is understated by these figures and thus it is important to understand why diagnostic radiological series do not mirror clinical practice.

Firstly, the confidence with which a radiological observation is made is a key component of its contribution to clinical diagnosis. In the three series in which the importance of observer confidence was evaluated, a confident diagnosis was made with CT scanning more often than with chest radiography; crucially, a confident diagnosis with CT scanning was almost always correct. This finding was most striking in the series of Mathieson et al, in which a confident diagnosis was made with CT scanning twice as often (89% vs chest radiography (23%); the accuracy of a confident first choice diagnosis with CT scanning was 95% compared with 77% for chest radiography. By contrast, when a first choice diagnosis was not made with high confidence, the advantage of CT scanning (60% accuracy in 51% of cases) over chest radiography (51% accuracy in 77% of cases) was less definitive (figures calculated from stated data). These results highlight the importance of taking into account the confidence of the radiologist in the clinical diagnosis of individual patients with interstitial lung disease. Diagnostic radiological series cannot quantify observer confidence with any precision; the designation of “high” and “low” confidence for CT observations, required for the purposes of a study, does not do justice to the shades of grey of radiological certainty in clinical practice.Appearances on a CT scan may be considered pathognomonic of a particular disease or the diagnosis may be highly probable, likely, or merely possible.

Nevertheless, the published radiological series of the late 1980s and early 1990s suggest that, in just over half of patients with diffuse infiltrative lung disease, a confident diagnosis, which is highly likely to be correct, will be made by an experienced CT radiologist. However, even this conclusion can now be challenged. Radiological experience has substantially increased over the last five years, and it is likely that the early diagnostic CT studies underestimate current radiological expertise. There is no better example of increasing radiological proficiency than the CT diagnosis of extrinsic allergic alveolitis (EAA), often an important differential in patients with suspected CFA. In early studies, a correct diagnosis was made in only 18 of 45 observations of patients with EAA, and a confident diagnosis was made in only 10%. However, since the early 1990s a CT picture considered virtually pathognomonic of subacute EAA has been recognised, consisting of widespread ground glass attenuation admixed with prominent regional decreased attenuation, enhanced on expiratory CT images. The diagnostic power of CT scanning has increased substantially in EAA and other diffuse lung diseases, simply as a result of greater radiological experience.

In another important respect, diagnostic radiological series cannot be extrapolated directly to clinical practice because they take no account of pre-test and post-test clinical probability, but are restricted to comparisons of diagnostic sensitivity between CT scanning and plain chest radiography in isolation. Purely radiological series of diffuse lung diseases cannot do justice to the act of clinical diagnosis which is not dependent upon CT scanning or chest radiography alone. A confident clinical diagnosis of an individual interstitial lung disease such as CFA is based upon a gestalt evaluation of clinical features at presentation, previous events (including the duration of history, initial environmental exposures, rate of progression and previous responsiveness to treatment), as well as investigations such as CT scanning and chest radiography. The clinical usefulness of CT scanning depends upon pre-test probabilities, the confidence (likelihood ratio) of the CT diagnosis, and thus the change in diagnostic probabilities resulting from the use of CT scanning. An appearance thought to be pathognomonic of CFA on CT scanning may have little impact on management when the diagnosis is already clinically obvious. By contrast, appearances which are merely suggestive may clinch the diagnosis of CFA if clinically feasible alternative diagnoses such as lymphangitis carcinomatosis are confidently excluded by CT scanning.

Thus, an appraisal of the true impact of CT scanning on the non-invasive diagnosis of CFA is essentially a statement of change in diagnostic perception. In only one series has this facet of the use of CT scanning been evaluated. Grenier and co-workers evaluated diagnostic sensitivities in individual diffuse lung diseases in a large group of patients based on clinical features alone, clinical features and chest radiography and, finally, clinical features in combination with chest radiography and CT scanning. It is worth examining this study in some detail because it illustrates the considerable difficulties in attempting this sort of analysis without recourse to a robust “gold standard”. Paradoxically, the sensitivity of a diagnosis of CFA was slightly lower with the addition of CT scanning (87%) than with chest radiography and clinical features alone (89%). However, this finding can be ascribed to the method of definition of a final “gold standard” diagnosis of CFA: diagnostic criteria consisted of typical clinical features in combination with characteristic chest radiographic findings in 35 of 46 cases. In essence, the evaluation of the diagnostic sensitivity of clinical features in combination with chest radiography amounted to an evaluation of clinical and radiological observer variation. Any change in diagnostic perception with the addition of CT scanning—for example, the confident diagnosis of an alternative diffuse lung disease—invariably led to deviation from the “final diagnosis” and hence to an apparent fall in CT diagnostic sensitivity. Thus, the pitfall of “diagnostic review bias”, well recognised in radiological studies, effectively invalidated the conclusions about patients with CFA in this study.

In theory, this problem might have been overcome by studying the diagnostic sensitivities of clinical features, chest radiography, and CT features in patients with a final histological
diagnosis of CFA. However, any such attempt inevitably falls foul of a second major bias, the problem of “sneaking technology”. CT scanning is now widely applied to clinical diagnosis and an increasing proportion of patients with CFA selected for open lung biopsy undergo the procedure because CT appearances are atypical or at odds with the clinical picture. Biopsied patients are increasingly unrepresentative of the larger population with CFA and investigations of this group are increasingly irrelevant to routine clinical diagnosis.

The difficulties in applying diagnostic CT series to routine practice are largely unavoidable. However, the clinical integration of CT scanning would have been facilitated by a more complete analysis of the accumulated data. As discussed above, CT scanning may play a crucial role in excluding individual diffuse lung diseases, especially when the clinician is able to reduce the likely differential diagnosis to CFA versus EAA, Langerhans cell histiocytosis, or lymphangitis carcinomatosis. In general, diagnostic CT series state the sensitivity and accuracy of CT scanning in the diagnosis of CFA are equally or more important in many clinical situations; however, in the only series of diffuse lung disease to attempt such statements26 the numbers of patients were too small to generate a convincing conclusion. There is a pressing need for definitive series documenting the overall diagnostic accuracy of the “pathognomonic” appearances of individual diseases.

This deficiency has been partially addressed in fibrosing alveolitis; in a group of 86 patients with a diffuse lung disease, including 45 with a final diagnosis of fibrosing alveolitis, CT appearances regarded as typical of CFA had a sensitivity of 88%, a specificity of 93%, and an accuracy of 91%.22 The series was compiled at a time when open lung biopsy specimens were taken routinely in patients with suspected fibrosing alveolitis, and the findings were robust in a large subgroup of 59 patients with a final histological diagnosis.23 However, results at referral centres, in this and other studies4–17 23 may overstate the accuracy of CT scanning in suspected CFA in routine clinical practice. The study population included scleroderma patients with lung involvement (in whom a histological diagnosis of fibrosing alveolitis is the rule) and CFA patients were largely referred with a progressive CFA-like course. Thus, in patients with an ultimate diagnosis of fibrosing alveolitis, the probability of that diagnosis prior to CT scanning was unusually high. The important conclusion to be drawn is that CT appearances typical of CFA are very likely to be accurate when associated with an intermediate to high pre-test diagnostic probability.

There is good circumstantial evidence that CT diagnosis is similarly accurate (and not merely sensitive) in many other diffuse lung diseases. The entity of “end stage diffuse lung disease” is a notoriously difficult diagnostic problem. Histological appearances and clinical features are non-specific and a histospecific diagnosis is often unattainable. However, CT scanning is a surprisingly powerful diagnostic tool in this context. In a study of 61 patients with “end stage diffuse lung disease”, the majority with a histological diagnosis earlier in the disease, the correct first choice diagnosis was made by CT scanning in 87% of patients and agreement between radiological observers was excellent.24 Thus, the documented ability of CT scanning to diagnose alternative diffuse lung diseases in patients with suspected advanced CFA (such as lymphangitis carcinomatosis, chronic extrinsic allergic alveolitis, and Langerhans cell histiocytosis) is a crucial consideration which is not addressed by statements about the sensitivity of CT scanning for the diagnosis of CFA.

The difficulties in applying radiological series to routine diagnosis are exacerbated by the nature of secondary populations. Diagnostic studies in interstitial lung disease are necessarily tertiary because sufficiently large numbers of patients can only be accumulated at referral centres. However, in secondary centres there is a lower prevalence of diffuse lung disease and a higher prevalence of heart failure, chronic infection, and metastatic malignancy than in tertiary populations. These disorders may simulate diffuse lung disease and sometimes cause considerable diagnostic difficulties in this regard, but are not well represented in diagnostic diffuse lung disease series. In particular, there is currently no large series evaluating the spectrum of CT manifestations of pulmonary oedema, but a number of anecdotal accounts of difficulties in distinguishing heart failure from alveolitis on CT scanning suggest that this problem is quite common. Thus, diagnostic series confined to patients with established interstitial lung disease do not simulate a larger dilemma faced by the clinician: the optimal use of CT scanning in diagnosis when suspected diffuse lung disease is part of a broader differential diagnosis.

A second issue pertinent to secondary centres is the vexed question of radiological experience. Experienced radiologists are understandably reluctant to commit themselves on the important question of what constitutes “minimum training” in the CT evaluation of diffuse lung disease as this partly depends upon the aptitude of the trainee radiologist. Whilst the same consideration applies equally to clinicians and histopathologists, the interpretation of CT patterns is a recent skill, often acquired by radiologists after the completion of formal training. Thus, the application of CT scanning to diagnosis must be tailored to local expertise, although it is reassuring that in a large series involving inexperienced observers the diagnostic advantage of CT scanning over chest radiography was robust.25 Fortunately, CT images are readily transportable and thus experienced radiologists at larger centres can play an invaluable role in offering second opinions in difficult cases. The review of biopsy specimens by a regional panel of pathologists with a particular interest in diffuse lung disease has recently been advocated26; using exactly the same logic, review of difficult cases by a panel
of experienced CT radiologists would help to standardise diagnosis and disseminate CT expertise. Thus, diagnostic CT series do not simulate clinical practice for diverse reasons. They fail to take into account the confidence of the radiologist in individual cases, the general increase in radiological expertise in the last five years, the modulating effect of pre-test clinical probability, and the value of CT scanning in excluding alternative histospecific diagnoses. They should not be extrapolated uncritically to radiological practice in secondary centres as they do not address the problems faced by less experienced CT radiologists and they do not include patients with other common disorders that may simulate diffuse lung disease clinically. However, despite their flaws, these series have stimulated the routine use of CT scanning in the diagnosis of CFA. The widespread application of CT scanning to clinical practice has led to a decrease in the performance of diagnostic open lung biopsy. Ironically, the most powerful evidence in support of this trend is circumstantial and negative. The use of CT scanning as a substitute for open lung biopsy in selected cases has not generally resulted in subsequent major management dilemmas. Exactly as CT scanning has replaced bronchography in the diagnosis of bronchiectasis by a process of clinical consensus, so it promises to obviate diagnostic lung biopsies in patients with a clinical and radiological picture entirely typical of CFA.

The use of CT scanning in suspected CFA is not confined to diagnosis; CT scans play a central role in the non-invasive evaluation of “disease activity” in fibrosing alveolitis. The separation of patients with CFA into subgroups with the histological appearances of usual interstitial pneumonitis and desquamative interstitial pneumonitis has been a consistent predictor of outcome; before CT scanning open lung biopsy was the sole reliable means of predicting survival and responsiveness to treatment.28 29 Chest radiography,30-32 bronchoalveolar lavage,3 and gallium scanning3 do not discriminate consistently between inflammatory and fibrotic disease. The clearance of inhaled 99mTc-DTPA has been used to distinguish between stable and progressive disease, but does not identify predominantly inflammatory disease; abnormally rapid clearance is seen equally in fibrotic disease and in patients subsequently responding to treatment.32 Similarly, individual lung function indices do not discriminate between predominantly inflammatory and predominantly fibrotic disease, whether defined at open lung biopsy33 or on CT criteria.34

In the majority of patients with fibrosing alveolitis, CT patterns are as accurate as histological appearances in predicting responsiveness to treatment. The histological significance of a reticular pattern in fibrosing alveolitis, denoting fibrosis, has been demonstrated repeatedly in CT-histological correlations35-38 and is now unquestioned. In one large study of serial CT appearances a reticular pattern was never seen to regress with treatment.39 The interpretation of a ground glass pattern is less straightforward. When ground glass attenuation predominates, it usually represents inflammatory cell infiltration40 and responds to treatment.41 42 However, when admixed with an equally extensive reticular pattern it is often associated with a poor prognosis;43 in this context, a ground glass pattern is probably indicative of fine fibrosis, although partial regression of disease with treatment is seen on serial CT scanning in a minority of cases.44 The prognostic use of CT scanning is analogous to the evaluation of open lung biopsy appearances; a good outcome is seen in 10–15% of cases alike with predominance of inflammatory cell infiltration on histological evaluation and with predominance of a ground glass pattern on CT scanning, but not in the majority with “mixed” or predominantly fibrotic, predominantly reticular disease. Recently, in a prospective study of 38 patients with biopsy proven CFA, CT appearances were more accurate than histological features in predicting a short term response to treatment; survival analyses were hampered by small numbers (a fatal outcome in only 10 patients) but suggested that the CT “fibrosis score” was as prognostically reliable as the histological severity of fibrosis or inflammation.45

The ease with which radiologists can designate CT appearances in CFA as a predominant reticular pattern, “mixed” disease, or a predominant ground glass pattern is an important consideration. In a large study of patients with fibrosing alveolitis the kappa coefficient of agreement between experienced radiologists of 0.5446 was typical of kappa values achieved in the interpretation of many routine radiological procedures.47 In a subsequent formal evaluation of interobserver variation in 128 patients with fibrosing alveolitis a similar kappa value (0.52) was observed.48 These values were considered to be suboptimal in a recent review of the clinical utility of thoracic CT scanning,49 but it should be stressed that the latter study overstated clinically important observer variation for two reasons. A large subset of patients with limited disease associated with systemic sclerosis was more difficult to categorise than patients with the more extensive disease seen in CFA. Secondly, much of the disagreement between observers lay between predominantly reticular and “mixed” disease which have a very similar prognosis. With the use of weighted quadratic system (equivalent to the intra-class correlation coefficient) which quantifies the degree of disagreement between observers,50 kappa values for interobserver variation for experienced observers rose to 0.72 in fibrosing alveolitis in general, and to 0.89 when analysis was confined to patients with CFA (unpublished data). Reassuringly, interobserver variation increased only marginally when observations made by two trainee radiologists (with little experience of thoracic CT scanning) were included in the analysis; furthermore, interobserver variation was minimal when radiological observations were made with high confidence. In most patients with CFA a reticular pattern
can readily be identified as the predominant CT abnormality, and thus a clinically useful evaluation of disease activity can be made by less experienced radiologists provided that observations made with low confidence are clearly identified to the clinician.

CT scanning offers a number of other clinical advantages in the management of CFA. The superior sensitivity of CT scanning in the detection of interstitial lung disease compared with chest radiography has been well documented in many disorders but is probably of relatively little value in CFA (which is usually radiologically overt at presentation). The ability of CT scanning to detect co-existing lung disease is of greater practical importance. Concurrent emphysema is common on CT scans but is seldom obvious on chest radiographs; the mixture of CFA and emphysema leads to spurious preservation of lung volumes but a devastating depression of gas transfer.

In this context, CT evaluation allows the clinician to make a more complete evaluation of the severity of fibrosing alveolitis than can be achieved with functional indices alone. Similarly, there is a high prevalence of lung cancer in CFA; malignant disease may be difficult to detect on chest radiography in the presence of extensive lung fibrosis but is usually evident on CT scanning (although small tumours may be missed on interspaced thin sections). Finally, some clinicians believe anecdotally that serial CT evaluation is a valuable adjunct to monitoring in selected cases, but the clinical usefulness of this use of CT scanning has yet to be formally evaluated.

The increasing use of CT scanning in the diagnosis and management of CFA has important implications for the performance of more invasive procedures such as BAL and open or thoracoscopic lung biopsy. The place of BAL in routine management is increasingly open to question. Advocates for BAL are inclined to argue that BAL findings add useful ancillary information in a minority of cases. However, with diagnostic CT studies, pre-test clinical probability has never been taken into account in a formal evaluation of the clinical usefulness of BAL; this consideration is increasingly important now that CT scanning has increased the diagnostic and prognostic information available in diffuse lung disease. Whether patients with CFA with a BAL lymphocytosis invariably have prominent ground glass attenuation on the CT scan has yet to be established. A prominent BAL neutrophilia is associated with extensive fibrotic disease on the CT scan in fibrosing alveolitis and thus it appears increasingly unlikely that this BAL finding adds significantly to the prognostic information gleaned from CT scanning. Similarly, it has yet to be established whether changes in diagnostic probability associated with certain BAL profiles add usefully to CT evaluation in patients with suspected CFA. For example, the diagnostic value of the marked lymphocytosis associated with active EAA may be of limited diagnostic value if it transpires that it is invariably associated with CT appearances virtually pathognomonic of subacute EAA and a compatible exposure history. It would be premature to discard BAL altogether in patients with suspected CFA, based on untested supposition, but formal evaluation of the added clinical value conferred by BAL, with a careful definition of pre-test probability, is now long overdue.

The impact of CT scanning on the performance of open or thoracoscopic lung biopsy is less straightforward. Historically, lung biopsy has been used in suspected CFA for diagnostic and prognostic purposes, and it is customary to refer to the procedure as a “gold standard”. However, it is in many respects an unsatisfactory one. The procedure is invasive, expensive, leads to delays in the institution of therapy and, unlike CT, cannot be performed serially to evaluate changes in disease activity. Many CFA patients with extensive disease are unfit for thoracotomy or thoracoscopy. Furthermore, interobserver variation has never been quantified in the histological diagnosis of diffuse lung disease despite the well recognised observer variation in other histological diagnoses, including the grading of malignancy. Review of the histological diagnosis is an integral part of the optimal management of diffuse lung disease; any clinician who has participated in this exercise is well aware that from time to time the “final histological diagnosis” does change. In this regard, the major observer variation documented between experienced pathologists in the assessment of the absolute severity of indices of fibrosis and inflammation in biopsy specimens taken from patients with CFA is not altogether reassuring.

However, despite its limitations, histological evaluation is undeniably crucial in some patients and the debate on the merits of CT scanning, as opposed to open lung biopsy, should not be viewed as an “either/or” proposition. In different ways, CT scanning and histological evaluation are both statements of lung morphology and the interpretative skills of radiologists and pathologists alike amount to pattern recognition. In the era of CT scanning the key question in individual patients is whether the results of a lung biopsy are likely to change management or refine statements about prognosis. It can now be cogently argued that, in patients with a clinical presentation typical of CFA (and thus a high pre-test probability), a highly compatible CT picture increases the probability of the diagnosis to such a level as to obviate the need for a biopsy. Clinicians who continue to advocate an automatic policy of taking lung biopsy specimens from patients with suspected CFA sometimes justify this approach by referring to occasional histological “surprises”. The overlap between CFA and chronic fibrotic EAA is often cited. In a recent CT study it was sometimes difficult to distinguish the two diseases (although it was not made explicit whether patients with chronic EAA were identifiable from exposure...
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Consolidation, an appearance very widespread ground glass attenuation and patchy NSIP the predominant features were widespread. For example, it has recently been reported that a histological diagnosis of non-specific interstitial pneumonia (NSIP) is associated with a much better outcome than CFA. The clinical and radiological features of NSIP have yet to be documented definitively, and the degree of clinical and CT overlap with CFA is uncertain. In the first CT description of NSIP the predominant features were widespread ground glass attenuation and patchy consolidation, an appearance very different from typical CFA; however, there are anecdotal reports of patients with histologically proven NSIP, including some known to the author, in whom CT appearances are indistinguishable from CFA. Thus, in occasional patients with a CT picture typical of CFA but evidence of a stable or slowly progressive process (based on historical features or stability on plain chest radiography), it can be argued that a histological diagnosis of NSIP may provide important prognostic information and alter the approach to treatment. Similarly, in younger patients (under the age of 45) in whom a diagnosis of CFA is at odds with the usual demographic features of the disease, thoracoscopic confirmation of the diagnosis may be warranted, especially if lung transplantation is contemplated. Thus, it is not yet clear whether the need for lung biopsies in the larger population of patients with diffuse lung disease will continue to diminish with the increasing use of CT scanning, or whether CT scanning will merely refine the future use of thoracoscopic procedures, strengthening the indications in a minority of cases.

In conclusion, the advent of CT scanning has had a major impact on the diagnosis and evaluation of disease activity in CFA. Although not a valid simulation of clinical practice, the landmark diagnostic CT series have stimulated the widespread use of CT scanning and this has led, in turn, to an increasing clinical consensus that the non-invasive diagnosis of CFA meets

"CFA" encountered in routine practice, studies of patients with CFA diagnosed non-invasively need to be encouraged. In conclusion, the advent of CT scanning has had a major impact on the diagnosis and evaluation of disease activity in CFA. Although not a valid simulation of clinical practice, the landmark diagnostic CT series have stimulated the widespread use of CT scanning and this has led, in turn, to an increasing clinical consensus that the non-invasive diagnosis of CFA meets...
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9 Weller Et al. Primack SL, Hartman TE, Hansell DM, et al. Life expectancy in patients with suspected CFA when clinical or CT features are atypical, but it is no longer justified to evaluate disease activity. The added diagnostic information provided by CT scanning should help patients to participate in management decisions and justifies the formal inclusion of CT scans in non-invasive diagnostic criteria in clinical studies.