CT of Sclerotic Bone Lesions: Imaging Features Differentiating Tuberous Sclerosis Complex with Lymphangiomyomatosis from Sporadic Lymphangiomyomatosis¹

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Purpose:

To determine if sclerotic bone lesions evident at body computed tomography (CT) are of value as a diagnostic criterion of tuberous sclerosis complex (TSC) and in the differentiation of TSC with lymphangiomyomatosis (LAM) from sporadic LAM.

Materials and Methods:

Informed consent was signed by all patients in this HIPAA-compliant study approved by the institutional review board. Retrospective analysis was performed of the body CT studies of 472 patients: 365 with sporadic LAM, 82 with TSC/LAM, and 25 with TSC. The images were reviewed by using a picture archiving and communication system workstation with bone settings (window width, 1500 HU; window level, 300 HU) and fit-to-screen option. CT image characteristics assessed included shape, size, and distribution of sclerotic bone lesions with subsequent calculation of differences in the frequency of these lesions.

Results:

Most commonly the sclerotic bone lesions were round, measured 0.3 cm (range, 0.2–3.2), and were distributed throughout the spine. The frequencies differed among the three patient groups. Four or more sclerotic bone lesions were detected in all 25 (100%) of those with TSC, with a sensitivity of .89 (72 of 82) and specificity of .97 (355 of 367) in the differentiation of sporadic LAM from TSC/LAM ($P < .01$).

Conclusion:

The number of sclerotic bone lesions at body CT is of potential value in the diagnosis of TSC and in the differentiation of patients with sporadic LAM from those with TSC/LAM.

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Lymphangioleiomyomatosis (LAM) can occur sporadically or in association with tuberous sclerosis complex (TSC), an autosomal dominant disorder with variable penetrance resulting from mutations in the *TSC1* and *TSC2* genes (1). Up to 35% of women with TSC have lung cysts that are identical histologically to LAM and are categorized as having TSC with lymphangioleiomyomatosis (hereafter, TSC/LAM) (1). It is important to distinguish patients with TSC/LAM from those with sporadic LAM, because TSC is an inherited disorder and genetic counseling may be of benefit (3). Furthermore, TSC is associated with disorders such as renal cell carcinoma, subependymal giant cell astrocytoma, and retinal astrocytomas for which early diagnosis may affect prognosis (2,3).

The diagnosis of TSC is usually made by observation of (a) family history of TSC; (b) characteristic dermatologic findings (eg, facial angiofibroma, periungual fibromas); and (c) findings at computed tomography (CT) or magnetic resonance (MR) imaging of the head and body that include cortical tubers, subependymal nodules, giant cell astrocytoma, lung cysts, and renal angiomyolipomas (2,4). The differentiation between sporadic LAM and TSC/LAM may prove to be difficult when the family history is unreliable or unavailable, the cutaneous stigmata of TSC are mild or absent, or CT or MR findings of the head are not available or are inconclusive (5).

Both patients with TSC/LAM and patients with sporadic LAM have lung

cysts and may have renal and/or hepatic angiomyolipomas and benign lymphatic masses, known as lymphangioleiomyomas, making their findings at body CT virtually indistinguishable (6,7). This difficulty in differentiating TSC/LAM from sporadic LAM according to chest and abdominal soft-tissue findings is reflected in the revised criteria for TSC, which require that “when both lymphangioleiomyomatosis and renal angiomyolipomas are present, other features of TSC should be present before a definitive diagnosis is assigned” (2,4).

Sclerotic bone lesions (SBLs) have been previously described as a diagnostic feature of TSC on radiographs (8–10). However, their potential as a diagnostic feature on CT scans has not been explored. In this study, we assessed the frequency of SBLs on body CT scans of patients with sporadic LAM, TSC/LAM, and TSC and evaluated the hypotheses that the presence of multiple SBLs at CT should be added to the diagnostic criteria of TSC and may be used as a differentiating feature between TSC/LAM and sporadic LAM.

Materials and Methods

Patients

Our retrospective study included 447 women with the diagnosis of LAM, of whom 82 also had TSC, and 25 patients (eight men, and 17 women) with TSC without evidence of LAM. The patients were seen between 1995 and 2007 as part of protocols 82-H-0032, 95-H-0186, and 96-H-0100 that evaluated the natural history of LAM, TSC/LAM, and TSC. The study protocols and consent

documents for the natural history studies were approved by our institutional review board. All subjects gave written informed consent before enrollment. The initial informed consent included consent for future retrospective analysis. Both the natural history protocols and our current retrospective analysis were compliant with the Health Insurance Portability and Accountability Act. The patients were referred by their local physicians, the LAM Foundation, or the Tuberous Sclerosis Alliance or they were self-referred.

In the 365 women with sporadic LAM, the diagnosis was established at biopsy of the lung in 231 patients and biopsy of abdominal or pelvic masses in 23 patients. The 111 of 365 patients without biopsy had classic clinical histories, such as recurrent spontaneous pneumothorax and/or chylous pleural effusions and specific CT findings (eg, diffusely scattered thin-walled lung cysts, renal angiomyolipomas) (6).

In the 82 women with TSC/LAM and the 25 patients with TSC, the diagnosis of TSC was made by means of established clinical and radiologic findings based on current consensus criteria that include dermatologic findings (eg, facial angiofibromas) and findings at

Advances in Knowledge

- Sclerotic bone lesions are significantly more common and numerous in patients with tuberous sclerosis complex (TSC) than in patients with TSC with lymphangioleiomyomatosis (LAM) and in patients with TSC/LAM than in patients with sporadic LAM.
- The number of sclerotic bone lesions is a useful feature in differentiating sporadic LAM from TSC/LAM and TSC.

Implications for Patient Care

- The number of sclerotic bone lesions seen at body CT is of value in the diagnosis of TSC and in the differentiation of patients with sporadic LAM from those with TSC/LAM.
- The CT finding of multiple sclerotic bone lesions might be added to the diagnostic criteria of TSC.

Published online

10.1148/radiol.09090227

Radiology 2010; 254:851–857

Abbreviations:

LAM = lymphangioleiomyomatosis
ROC = receiver operating characteristic
SBL = sclerotic bone lesion
TSC = tuberous sclerosis complex

Author contributions:

Guarantors of integrity of entire study, N.A.A., J.M.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; literature research, N.A.A., A.R., C.H.H., J.M.; clinical studies, N.A.A., A.R., T.D., C.H.H., J.M.; experimental studies, A.R., C.H.H., J.M.; statistical analysis, A.J.D., C.H.H.; and manuscript editing, N.A.A., A.J.D., A.R., C.H.H., J.M.

Funding:

A.R. and J.M. are employees of the National Heart, Lung, and Blood Institute.

Authors stated no financial relationship to disclose.

brain CT and/or MR imaging (eg, subcortical brain hamartomas or “tubers”) (2,4). In the 82 patients with TSC/LAM, the diagnosis of LAM was established at lung biopsy in 26 patients and lymph node biopsy in two patients. The 54 patients without tissue biopsy had the classic clinical histories and CT findings of LAM noted above.

Imaging

All patients underwent CT of the chest, abdomen, and pelvis with contiguous 5-mm-thick sections by using HiSpeed Advantage, CTi, or LightSpeed scanner (GE Medical Systems, Milwaukee, Wis) and a MX 6000 CT unit (Philips, Cleveland, Ohio) with automatic tube current modulation or with 240 mA and 0.8-second rotation time, 120 kV, field of view of 36 cm, and a pitch of 0.8–1.0.

Image Analysis

The images were reviewed by an observer (N.A.A.) with more than 20 years experience in CT during multiple separate reading sessions using a picture archiving and communication system (5.1; Kodak, Rochester, NY) with bone settings (window width, 1500 HU; level, 300 HU) and fit-to-screen viewer option, which gives a full-screen display of the image. The reviewer was aware of the patients' sex and whether they had sporadic LAM or TSC but not whether the patients had LAM in combination with TSC. The studies of five to 10 patients were reviewed per session for a total of at least 60 separate reading sessions. For each patient, the number and anatomic location of SBLs within the skeleton were recorded. Five patients in each group (sporadic LAM, TSC/LAM, and TSC) were randomly chosen, and the size and shape of the SBLs were recorded. The lesions were measured with electronic calipers, and only one measurement was performed of each lesion. Imaging characteristics that were evaluated included whether the bone lesion deformed or extended beyond the cortex of the bone in which it resided and whether the bone lesion extended across the entire width of the bone and acquired the shape of the bone. One patient with LAM and breast cancer

Table 1

CT Characteristics of SBLs in 15 Randomly Selected Patients with LAM, TSC, or TSC/LAM

Characteristic	LAM (n = 5)	TSC/LAM (n = 5)	TSC (n = 5)
No. of lesions	40	63	353
Mean size (cm)*	0.4 (0.2–1.4)	0.4 (0.2–3.2)	0.3 (0.2–1.5)
Shape†			
Round	36 (88)	53 (83)	314 (88)
Oblong	1 (0.03)	7 (0.1)	28 (0.08)
Rectangular	0	3 (0.05)	8 (0.02)
Flame	3 (0.08)	0	3 (0.01)

* Data in parentheses are the range.

† Data in parentheses are the percentages.

Figure 1

Figure 1: CT scan in a 47-year-old woman with TSC/LAM. Axial section at the T4 level viewed with bone windows demonstrates multiple sclerotic round bone lesions (arrows) in the vertebral body, right transverse process, and left rib.

had multiple lytic and blastic bone lesions characteristic of metastatic breast cancer and was excluded from the analysis.

Clinical Chart Review and Dermatologic Examination

The clinical charts of all 82 patients with TSC/LAM, reports from MR imaging of the head (76 of 82) and echocardiogram (24 of 82), were reviewed by a nurse practitioner (A.R.). The patients also underwent dermatologic examinations by a board-certified dermatologist (T.D.) evaluating the patients for cutaneous stigmata of TSC. These findings were tabulated to further assess the potential use of SBLs in the evaluation of patients with TSC.

Statistical Analysis

The cumulative probability distributions of the numbers of SBLs were determined for patients with sporadic LAM, TSC/LAM, and TSC. These were compared by means of the Komolgorov-Smirnov test. The sensitivity, specific-

ity, and positive and negative predictive values of having more than four SBLs in the diagnosis of TSC were determined. Receiver operating characteristic (ROC) curves were plotted, and the areas under the ROC curve were calculated. Spearman rank correlation coefficients were calculated between age and numbers of SBLs in each patient group.

Results

The distribution of sizes and shapes of the 456 SBLs in 15 randomly selected patients with sporadic LAM, TSC/LAM, and TSC are shown in Table 1, and the most frequent appearance is illustrated in Figure 1. The SBLs ranged in size from 0.2 cm to 3.2 cm. None expanded the bone, deformed, or extended beyond the cortex; hence, the shape of a lesion was related to its size and proximity to the cortex of the bone. The majority were round. Rarely, the lesions had a flame shape; this pattern was most commonly seen in the sacrum

Figure 2: CT scan in a 38-year-old woman with LAM. Axial section through the pelvis viewed with bone windows shows single flame-shaped lesion in the right iliac bone (arrow).

and pelvis (six of 456, 1.3%) (Fig 2). Those large enough to extend across the entire width of the bone acquired the contours of the bone in which they resided; this was seen most commonly with lesions in the posterior elements of the spine conforming to the shapes of the pedicle, lamina, transverse process, or spinous process and exhibiting a rectangular shape (11 of 456, 2.4%) (Fig 3).

The distribution of the numbers of SBLs per patient differed among the patients with sporadic LAM, TSC/LAM, and TSC (Table 2 and Fig 4). SBLs were more numerous in patients with TSC/LAM than in patients with sporadic LAM ($P < .01$, Kolmogorov-Smirnov test) and more numerous in patients with TSC in the absence of LAM than in patients with TSC/LAM ($P < .01$, Kolmogorov-Smirnov test). The numbers of SBLs per patient ranged from zero to nine in patients with LAM; whereas 49 of 82 (60%) patients with TSC/LAM and 22 of 26 (85%) patients with TSC had 10 or more lesions, and some had over 100 lesions (Fig 4).

The distribution of the patients' ages was similar among the three groups: for those with sporadic LAM, the median age was 43 years $\pm$ 9.1 (standard deviation) (range, 21–77 years); for those with TSC/LAM, the median age was 39 years $\pm$ 10.0 (range, 18–62 years); and for those with TSC, the median age was 43 years $\pm$ 15.4 (range, 19–72 years). Hence, the observed difference in the numbers of SBLs among the groups is not the result of differences in patient

Table 2

Distribution of the Number of SBLs in LAM, TSC/LAM, and TSC

No. of Bone Lesions	LAM (<i>n</i> = 364)	TSC/LAM (<i>n</i> = 82)	TSC (<i>n</i> = 25)
None	257 (71)	5 (6)	0
One or more	110 (30)	80 (98)	25 (100)
Four or more	10 (3)	72 (88)	25 (100)
Ten or more	0	49 (60)	22 (88)

Note.—Data in parentheses are the percentages.

Figure 3: CT scan in a 43-year-old woman with TSC/LAM. Axial section at the T8 level demonstrates rectangular-shaped SBLs conforming to the shape of the bones but not expanding them in the pedicle (white arrow), transverse process (arrowhead), and right rib (black arrow). Note three coalescing round lesions in the anterior aspect of the vertebral body.

Figure 4

Figure 4: Graph depicts cumulative probabilities of the numbers of SBLs in 364 patients with LAM, 82 patients with TSC/LAM, and 25 patients with TSC.

age. The conclusion that age is not a factor in the number of SBLs is further supported by the results of the correlation analysis, which demonstrated negligible, statistically insignificant, association between patients' ages and the numbers of SBLs in each patient group ($\rho = -0.008$, $P = .8$ for the sporadic LAM group; $\rho = 0.03$, $P = .8$ for the

TSC/LAM group; and $\rho = -.17$, $P = .4$ for the TSC group).

The ROC analysis demonstrated excellent separation between those with sporadic LAM and those with TSC/LAM in terms of the numbers of SBLs, with the area under the curve of 0.96 (Fig 5). Four or more SBLs were detected in 72 of 82 (88%) of those

Figure 5

Figure 5: Empirical ROC curve demonstrates data of patients with TSC/LAM from those with sporadic LAM in terms of the number of SBLs seen at CT of the chest, abdomen, and pelvis. Area under the curve of 0.96 indicates high discriminating ability. The criterion of four or more SBLs in a patient (arrow) has sensitivity of 0.89 and specificity of 0.97 for TSC/LAM versus LAM. *FPR* = false-positive rate, *TPR* = true-positive rate.

Figure 6

Figure 6: Empirical ROC curve demonstrates data of patients with TSC from those with sporadic LAM in terms of number of SBLs seen at CT of the chest, abdomen, and pelvis. Area under the curve of 0.99 indicates high discriminating ability. The criterion of four or more SBLs in a patient (arrow) has sensitivity of 1.0 and specificity of 0.97 for TSC versus LAM. *FPR* = false-positive rate, *TPR* = true-positive rate.

with TSC/LAM and in 10 of 364 (3%) of those with sporadic LAM. Of the 446 patients with LAM, 82 had TSC/LAM (ie, prior probability of TSC/LAM = 0.18). In those patients with four or more SBLs, the probability of TSC/LAM increased to 0.89 (72 of 82) and in those patients with three or fewer SBLs, the probability of TSC/LAM decreased to 0.03 (10 of 365).

Table 3

Anatomic Distribution of SBLs in the Skeleton in Patients with Four or More Lesions

Anatomic Site	LAM (<i>n</i> = 10)	TSC/LAM (<i>n</i> = 72)	TSC (<i>n</i> = 25)
Thoracic spine	7 (70)	72 (100)	25 (100)
Lumbar spine	4 (40)	60 (83)	20 (80)
Sacrum	10 (100)	55 (76)	20 (80)
Pelvis	5 (50)	46 (64)	19 (76)
Ribs	0	16 (22)	10 (40)
Femur head	4 (40)	17 (24)	11 (44)
Sternum	0	4 (6)	7 (28)
Humerus head	1 (10)	6 (8)	5 (20)
Scapula	1 (10)	6 (8)	2 (8)
Clavicle	0	0	2 (8)

Note.—Data in parentheses are the percentages.

Table 4

Distribution of SBLs in the Spine in Patients with Four or More Lesions

Distribution	LAM (<i>n</i> = 10)	TSC/LAM (<i>n</i> = 82)	TSC (<i>n</i> = 25)
Body	7 (70)	67 (82)	23 (92)
Pedicle	3 (30)	61 (74)	20 (80)
Lamina	2 (20)	56 (68)	23 (92)
Transverse process	1 (10)	54 (66)	18 (72)
Spinous process	1 (10)	33 (40)	14 (56)

Note.—Data in parentheses are the percentages.

Hence, for distinguishing patients with sporadic LAM from patients with TSC/LAM, the cut-off diagnostic criterion of four or more SBLs for TSC/LAM had a sensitivity of 0.89, specificity of 0.97, positive predictive value of 0.85, and negative predictive value of 0.02.

The ROC curve for sporadic LAM versus TSC demonstrated even better separation between the two groups (area under the curve, 0.99) in terms of the numbers of SBLs (Fig 6). Four or more SBLs were detected in all 25 (100%) patients with TSC. Of the 389 patients in the analysis with sporadic LAM or TSC, 25 had TSC (ie, prior probability of TSC = 0.06). In those patients with four or more SBLs, the probability of TSC increased to 0.71 (25 of 35), and in those patients with three or fewer SBLs, the probability of TSC decreased to 0 (0 of 352). Hence, in the context of distinguishing patients with sporadic LAM from patients with TSC, the cut-off diagnostic criterion of

four or more SBLs had a sensitivity of 1.0, specificity of 0.97, positive predictive value of 0.86, and negative predictive value of 0 for TSC.

The anatomic distribution of SBLs in the 107 patients with four or more SBLs is shown in Table 3. Tabulated are the numbers of patients with at least one SBL in the specific anatomic region. SBLs are invariably found in the spine and commonly in the pelvis—every patient in each group had at least one in the thoracic or lumbar spine or sacrum; however, SBLs were also found in ribs and/or sternum, proximal femora, and humeri. Within the spine, SBLs were seen in all anatomic components: the vertebral bodies, pedicles, and posterior elements (Table 4).

As shown in Table 5, in our patient population the presence of four or more SBLs at body CT was the third most common imaging finding (after cortical tubers and renal angiomyolipoma) in TSC/LAM and more common

Table 5

Clinical and Imaging Findings in Patients with TSC/LAM

Examination and Finding	No. of Patients with TSC/LAM
Body CT (n = 82)	
Renal angiomyolipoma	74 (91)
Four or more SBLs	72 (88)
Fatty liver tumor	28 (34)
Lymphangioleiomyoma	11 (13)
Head MR (n = 76)	
Cortical tubers	72 (95)
Subependymal nodules	47 (62)
Giant cell astrocytoma	9 (12)
Echocardiogram (n = 24)	
Cardiac rhabdomyoma	1 (4)
Family history (n = 75)	
TSC	29 (39)
Medical history (n = 79)	
Seizures	38 (48)
Dermatologic examination (n = 58)	
Facial angiofibroma or forehead plaque	56 (97)
Ungual/periungual fibroma	53 (91)
Dental pitting	51 (88)
Hypomelanotic nodules	43 (74)
Shagreen patch	40 (69)
Gingival fibroma	24 (41)
Confetti spots	15 (26)

Note.—These patients had undergone examinations or have records available for review for a given imaging or clinical examination. Data in parentheses are the percentages.

than some of the dermatologic findings (gingival fibromas, hypomelanotic nodules, shagreen patches, and “confetti” lesions) used as criteria in the diagnosis of TSC (4).

Discussion

The presence of four or more SBLs at body CT differentiates patients with sporadic LAM from those with TSC/LAM or TSC, with high sensitivities (89%, 100%) and specificity (97%). SBLs were the third most common imaging finding in these patients after brain tubers and renal angiomyolipomas. With the exception of facial angiofibroma or forehead plaque, dental pitting, and ungual/periungual fibroma, we found that SBLs were more common

than other findings obtained at physical examination (Shagreen patch, hypomelanotic nodules, “confetti” spots, and gingival fibroma) that are routinely used as diagnostic criteria for TSC (2,4). The frequencies of dermatologic findings in our study were similar to those in the literature, with exceptions related to age-dependent occurrence of lesions. Our patient population was unlike many in the literature: all our patients were adults, whereas most published TSC cohorts consisted predominantly of children. Therefore, lesions that occur later in life such as periungual fibromas were more frequent in our study than in most studies (91% versus 68%), while lesions that tend to become less apparent over time such as hypomelanotic nodules had lower frequency in our study than reported in the literature (74% vs 97%) (8). Hence, the presence of four or more SBLs is potentially useful as a diagnostic feature for TSC in the assessment of patients with LAM—the greater the number of SBLs, the more confident one may be of the diagnosis of TSC. SBLs are invariably found in the spine but may be found in any portion of the axial skeleton; hence, review of the CT examination of the ribs, sternum, and pelvis in addition to the spine is needed to accurately assess the number of SBLs.

In 1967, Komar et al (9) published the results of their review of the literature of the radiographic bone findings in TSC and their assessment of the lumbosacral spine and pelvis in 58 patients. Our results agree with theirs on several points: most of the lesions are round or oval in appearance—similar in appearance to bone islands/enostoses—and some are flame shaped; many different bones can be affected; and extensive involvement in the proper setting is “virtually diagnostic” of the presence of TSC. We observed a higher prevalence of SBLs than authors of this prior work; this is likely due to the improved depiction of bone structure and increased sensitivity to bone lesions provided with CT.

TSC is associated with hamartomas of the brain, skin, and heart (2). SBLs seen in TSC may represent another

manifestation of an underlying hamartomatous process, but there is scant literature on the histopathology of SBLs in TSC (10,11). Since SBLs usually do not produce symptoms, patients do not undergo biopsy (9). In 1952, Holt and Dickerson (12) reported the results of a biopsy of a SBL in the diploe of the skull in a patient with TSC. They found that the marrow spaces of the cancellous bone had been replaced by a concentric deposition of bone on preexisting trabeculae.

Radiologically, the SBLs in TSC closely resemble bone islands (enostoses), foci of dense, compact bone within the medullary cavity of bones (9). Histologically, bone islands consist of a dense network of thick compact mature bone trabeculae surrounded by normal spongiosa and have been considered hamartomatous lesions of no clinical importance (11). Onitsuka (13), in a review of radiographs in 189 healthy subjects, found that the prevalence of rib and pelvic bone islands was 0.43% and 1.08%, respectively. However, the anatomic and frequency distributions of bone islands at CT in the general population have not been established.

Multiple SBLs are seen in other conditions in addition to TSC and TSC/LAM. The differential diagnosis of SBLs includes osteoblastic metastasis, osteopoikilosis, and mastocytosis (14,15). Nevertheless, in the evaluation of patients with LAM or suspected of having TSC, the presence of multiple SBLs remains useful in establishing the presence of LAM/TSC or TSC. This is because in this clinical setting, the pretest probability of TSC is higher than the pretest probabilities of these other SBL-causing entities. Hence, according to the Bayes theorem, given a patient with multiple SBLs in this setting, the posttest probability of TSC/LAM or TSC is high.

A limitation of this study was the lack of a control group of patients with neither LAM nor TSC/LAM. This brings to question the validity of extrapolation of the results of this study to the evaluation of patients suspected of having TSC in the general population. We suggest, however, it is likely that SBLs are seen with less or equal frequency and

number in patients without LAM than in patients with sporadic LAM. Thus, the ability of using multiple SBLs to distinguish patients with TSC from those without TSC in the general population is likely greater than the ability to distinguish patients with TSC/LAM from patients with sporadic LAM, as demonstrated in this study. Another limitation of this study was that the detailed assessment of bone lesions was only made in a small subset of patients, that is, in five patients from each of the three patient groups with LAM, TSC/LAM, and TSC. Given that some patients had more than 100 lesions, evaluation of a larger group of patients became impractical. Despite this, 456 SBLs were analyzed.

The revised criteria currently recommended by the Tuberous Sclerosis Alliance for the diagnosis of TSC include lytic bone lesions as a minor diagnostic feature of TSC but do not include SBLs (2,4). The lytic bone lesions used in the criteria are small cortical cysts with sclerotic rims that contain fibrous tissue (12,16,17). These lesions are present in approximately 60% of patients with TSC, but since they are most commonly found in the metacarpals and metatarsals, radiographs of the extremities are required for their evaluation (9,16). In contrast, the SBLs described in this report have a higher prevalence in TSC than the bone lesions included in the current diagnostic criteria for TSC. Also, they are easily diagnosed by examining the bone windows from existing CT data, and thus do not require additional radiographs for their evaluation.

Before the introduction of the picture archiving and communication system, review of the skeletal structures on CT scans required that images be filmed with bone window settings. With the advent of the picture archiving and communication system, review of CT images with bone windows has become

a simple task. A click of a computer key allows inspection of images with bone window settings and quick determination of whether bone lesions are present.

SBLs evident on CT scans are more common and numerous in patients with TSC or TSC/LAM than in patients with sporadic LAM. Identification of four or more SBLs in patients with LAM markedly increases the likelihood of associated TSC—the greater the number of SBLs the more confident the diagnosis of the presence of TSC. When evaluating patients with LAM at CT, bone windows should be examined to search for sclerotic, or as previously described, lytic bone lesions. Any patient with LAM who is found to have multiple SBLs at CT should have a complete evaluation for TSC. The high prevalence of multiple SBLs in patients with TSC/LAM and TSC suggests that it be added to the diagnostic criteria of TSC.

Acknowledgments: We thank the LAM Foundation and the Tuberous Sclerosis Alliance for patient referrals.

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