## **Appendix E1**

**Skewness** is the third statistical moment of the grey-level histogram and is computed as follows:

skewness: 
$$\frac{w_3}{w_2^{3/2}}$$
,  $w_k = \sum_{i=0}^{s_{\text{max}}} n_i (i - \overline{i})^k / N$ ,  $N = \sum_{i=0}^{s_{\text{max}}} n_i$ ,  $\overline{i} = \sum_{i=0}^{s_{\text{max}}} (in_i / N)$ ,

where  $n_i$  is the number of times that grey-level value *i* occurs in the image region,  $g_{\text{max}}$  the maximum grey-level value, and *N* the total number of image pixels (24,26).

**Coarseness** computation is based on the neighborhood grey tone difference matrix (26,44) of the grey-level values within the image region, which is derived by estimating the difference between the grey-level value of each pixel and the average grey-level value of the pixels around a neighborhood window as follows:

$$coarseness:\left(\sum_{i=0}^{g_{\max}} p_i v(i)\right)^{-1} \text{ and } v(i) = \begin{cases} \sum \left|i - \overline{L}_i\right| \text{ for } i \in \{n_i\} \text{ if } n_i \neq 0\\ 0 \text{ otherwise} \end{cases},$$

where v(i) is the neighborhood grey tone difference matrix. In the above equations,  $g_{max}$  is the maximum grey-level value,  $p_i$  the probability that grey level *i* occurs, and  $\{n_i\}$  the set of pixels having a grey-level value equal to *i*.  $\overline{L_i}$  is given by

$$\overline{L}_i = \frac{1}{S-1} \sum_{k=-t}^t \sum_{l=-t}^t j(x+k, y+l),$$

where j(x,y) is the pixel located at (x,y) with grey-level value i,  $(k,l) \neq (0,0)$  and  $S = (2t + 1)^2$  with t = 1 specifying the neighborhood size around the pixel located at (x,y).

**Contrast, energy, and homogeneity**, as proposed originally by Haralick et al (45), require the computation of second-order statistics derived from the grey-level cooccurrence matrix, in which the spatial dependence of grey levels is estimated by calculating the frequency of the spatial co-occurrence of grey levels in the image (45).

Contrast = 
$$\sum_{i=0}^{g_{\text{max}}} \sum_{j=0}^{g_{\text{max}}} |i-j|^2 C(i,j)$$
, energy =  $\sum_{i=0}^{g_{\text{max}}} \sum_{j=0}^{g_{\text{max}}} C(i,j)^2$ , and homogeneity =  $\sum_{i=0}^{g_{\text{max}}} \sum_{j=0}^{g_{\text{max}}} \frac{C(i,j)}{1+|i-j|}$ ,

where  $g_{\text{max}}$  is the maximum grey-level value and *C* the normalized co-occurrence matrix (45). To optimize the computation of the grey-level co-occurrence statistics, grey-level quantization was implemented. Several grey-level quantization algorithms have been proposed in the literature (23,24,47). In our study, based on our preliminary evaluations reported previously (35,47), the range of the original grey-level values  $N_g$  in each ROI is linearly scaled to a smaller range of  $N_G$  grey-level values (ie,  $N_G < N_g$ ) (47). All ROIs are quantized to the same degree, with each ROI being quantized relative to its original range of grey-level values  $N_g$ . A range of different parameters is evaluated for  $N_G$  (ie,  $N_G =$ 

 $N_g/4$ ,  $N_g/8$ ,  $N_g/16$ ,  $N_g/32$ ,  $N_g/64$ ,  $N_g/128$ ). After grey-level quantization, the co-occurrence frequencies are calculated symmetrically in the four directions around each pixel by using a displacement vector d = (dx, dy) along x and y dimensions, where  $dx = \{0,1\}$  and  $dy = \{0,1\}$  to define 1 pixel offset in each direction. The four corresponding texture features calculated in each of these directions are averaged to create a single measure that is used in our experiments.

**Fractal dimension** can be estimated on the based on the power spectrum of the Fourier transform of the image as previously reported (46,83) and used in our preliminary studies (35). The two-dimensional discrete Fourier transform was performed by using the fast Fourier transform algorithm as follows:

$$F(u,v) = \sum_{m=0}^{M-1} \sum_{n=0}^{N-1} I(m,n) e^{-j(2\pi/M)um} e^{-j(2\pi/N)vn}, \quad u = 0, 1, \dots, M-1 \quad v = 0, 1, \dots, N-1,$$

where *I* is the two-dimensional image region of size (M, N), and *u* and *v* are the spatial frequencies in the *x* and *y* directions, respectively. The power spectral density *P* was estimated from F(u,v) as follows:

$$P(u,v) = |F(u,v)|^2.$$

To compute the fractal dimension, *P* is averaged over radial sections spanning the fast Fourier transform frequency domain. The frequency space is uniformly sampled in 24 directions, with each direction subsequently sampled uniformly at 30 points along the radial component, resulting in a total of 720 samples (ie, data points) of the frequency space. To calculate the fractal dimension the least squares fit of the log(*P<sub>f</sub>*) versus log(*f*) is estimated, where  $f = \sqrt{u^2 + v^2}$  denotes the radial frequency (83). The fractal dimension (*FD*) is related to the slope  $\beta$  of this log-log plot by

$$FD = \frac{3D_T + 2 - \beta}{2} = \frac{8\beta}{2}$$

where  $D_T$  is the topological dimension and is equal to 2 for a two-dimensional image.