There are two ways to test therapy for atherosclerosis in man: trials which measure cardiovascular death rates and trials that measure the rate of change in atherosclerotic lesions. Mortality-based trials require large study groups and relatively long periods of observation. Lesion tracking trials require fewer study subjects and shorter periods of observation, but are dependent on valid reliable assessment of lesion changes. To date, coronary angiography has been the major endpoint measure used in lesion trials. This review covers factors which influence the performance of angiography.

Inherent limitations to x-ray imaging include image mottling caused by a combination of x-ray noise and non-uniform blood contrast mixing, which is a major problem when only single frames of cine angiograms are measured, as is the case in most trials to date. Efforts to reduce the effect of image mottling have included spatial filtering, averaging of densitometric profiles from adjacent scanlines along a segment, or averaging of diameter profiles from sequential cine frames. Measurement of multiple frames during the cardiac cycle has been proposed by Spears and Selzer. Figure 1 shows a plot of diameter and stenosis measurements over two cardiac cycles for a segment of an unbypassed circumflex artery and illustrates the effect of frame averaging on four computer derived measures {D(90), D(3), DAVG, and % Diameter Stenosis} in 100 sequential frames of a left circumflex coronary artery. The darker lines show diameters after 5 point averaging filter. In theory, measurement error due to random effects, such as quantum mottle and contrast mixing, should be reduced in proportion to the number of averaged frames. In practice, three sequential frames appears to be the best number to average because of vessel motion during the cardiac cycle.

Other limitations to angiography are of biological origin, such as differences in vasomotor tone and vessel motion and non-uniformity of blood contrast mixing. The latter has been shown to strongly affect both visual and automatic edge tracking. Changes in size of the vessel image during the cardiac cycle have been attributed to differential magnification from vessel translation or rotation, pressure increase due to the injection itself, and arterial pressure pulsation. Periodic variations in vessel diameter have been shown in both animals and man which are of the same order of magnitude as annual progression/regression rates of atherosclerosis. In addition, from the work of Glagov et al. it is known that because of compensatory vessel wall dilatation coronary artery stenosis...
Quantitation of atherosclerosis has been by panels of human readers and computer-assisted quantitation or computerized image processing. For computer-assisted quantitation, coronary angiograms are projected and vessel outlines are hand traced with a digitizing stylus after which lesion severity is calculated by computer. Manual edge tracking is subject to inter-observer and intra-observer variability due to the subjective process of locating the vessel edge within the penumbra appearing on the film. For computerized image processing, selected frames from the cinefilm are digitized with a video camera and computer programs are used to locate the vessel edges and estimate the extent of lesions. Published estimates indicate that the precision of the automatic edge tracking method is about twice that of manual tracing. However, human performance factors influence results from the most advanced automated edge tracking procedures in current use because humans must select lesions or vessel segments for processing.

When film reading conditions are optimized, two member panels of human readers are quite adequate in obtaining comprehensive lesion counts which are important in studies of new lesion formation but difficult to obtain by computer because current programs do not track vessels well at branch junctions. Humans also outperform computers for integration of change in...