Atherosclerosis of the arteries in the human is a pathological process with serious consequences. It results in loss of elasticity of vessel walls, in focal development of plaques, and in irregular narrowing of the arterial lumen. The resultant impairment of blood flow may lead to heart attack, stroke, or gangrene of the limbs. The currently acceptable clinical method for providing the best quantitative measures of the extent of atherosclerotic lesions is angiography, which is time-consuming and expensive and which also carries a small but significant risk to the patient. Subjective interpretations of the angiogram and projection errors result in variability in sensitivity and specificity. Image-processing techniques may overcome some of the problems, but inconsistencies remain. Furthermore, the invasiveness of the procedure generally precludes repeat angiograms at frequent intervals.

In a number of research laboratories, noninvasive methods are currently being explored as alternatives to angiography, and ultrasonic methods are being used in a few clinical centers for peripheral artery studies. The potential benefits of noninvasive quantitative assessments include determination of the need for therapy and evaluation of the progression or regression of lesions by serial examinations, with virtually no risk to the patient. Furthermore, if noninvasive quantitative measures prove to be at least as reliable and sensitive as those obtained by angiographic techniques, clinical trials to assess the efficacy of measures for the prevention or treatment of atherosclerotic lesions could be conducted with many fewer patients than are now needed for meaningful results.

In January 1980, the National Heart, Lung, and Blood Institute convened a Workshop on Noninvasive Techniques for Assessment of Atherosclerosis in Peripheral, Carotid, and Coronary Arteries. Presentations and discussions included the potentials and limitations of ultrasound, radiography, nuclear magnetic resonance, gamma and positron emission tomography, and microwave techniques for imaging and assessing atherosclerotic lesions in arteries. The chemical and structural characteristics of the atheromatous plaque were also discussed. This synopsis of the workshop recommendations highlights important recent advances with the hope of encouraging researchers to explore areas with high potential for success in the noninvasive detection and characterization of atherosclerotic lesions. The full proceedings of the workshop will be published in the near future.

The two noninvasive modalities that currently provide the most reliable information and greatest application are: 1) enhanced radiographic techniques using intravenous injection of contrast agents; and 2) ultrasonic. Ultrasound B-scan modes combined with Doppler flow systems are now capable of visualizing atherosclerotic lesions in carotid arteries. Several studies indicate that this method can detect smaller lesions with greater precision than angiographic methods. The ability to obtain both transverse and longitudinal images of lumina and lesions with the B-scan mode is a distinct advantage over angiographic views. The Doppler flow data provide information about flow abnormalities that may indirectly indicate plaque surface characteristics. Ultrasound can successfully reveal peripheral arteries that are 2 to 4 cm below the skin surface, but radiologists using this modality encounter severe problems with deeplying peripheral arteries as well as with coronary arteries.
Radiographic methods using computed subtraction in conjunction with intravenously injected contrast agents in two views have demonstrated the feasibility of imaging lumina of carotid and peripheral arteries. This technique has the potential for providing the same information as current angiographic techniques but carries significantly less risk for the patient since intraarterial injections are not required. Preliminary studies indicate that this method has the potential for visualizing lumina of the coronary arteries with a resolution of fractions of 1 mm. However, the motion of the subject and the heart during the procedure and a low signal-to-noise ratio due to the background of the ventricular blood volume present problems needing solution.

Both ultrasonic and intravenous radiographic techniques are in a state of rapid technological development. In ultrasonic methods, improvement of transducers, dynamic focusing, and use of higher frequencies have the potential for significantly improving resolution and visualizing the lumina of deep-lying arteries. Reflected ultrasonic energy contains information on tissue characteristics as well as on ranges; thus, there is a potential for characterizing lesion composition. In the future, for example, spectral analysis of ultrasonic B-scans may permit determination of lipid content or calcium content on the basis of reflectivity, absorption, or scattering of the received energy. The possibility of using an ultrasonic probe at the tip of an esophageal or intravenous catheter may lead to improved capability for detection and characterization of lesions in coronary and other deep-lying arteries.

In contrast to ultrasound, intravenous radiographic methods image arterial lumina rather than the detailed structure of arterial walls or lesions, and therefore cannot characterize lesion composition using current techniques for energizing x-ray sources. However, the potential for doing this may be on the horizon if two or three monoenergetic beams are used in computed tomography (CT) scanning. For imaging coronary or other deep-lying arteries, intravenous radiographic techniques are less severely limited by poor transmission than is ultrasound. Specific areas of research that may result in improved image quality using intravenous radiography include work on image intensifiers with greater sensitivity and dynamic range, new radiographic contrast materials, improved computer algorithms for image reconstruction, and monoenergetic x-ray sources. Improvements in injection catheters and lower cost mass storage media will also be valuable.

Use of positron emission tomography for assessing atherosclerosis is, for the most part, in an earlier technological stage than either radiography or ultrasound. Precise localization and characterization of atherosclerotic lesions cannot presently be achieved with this method since tracers that localize specifically in the plaque region are not available. However, this modality has demonstrated potential for measuring specific volume flow in the human myocardium and can detect infarctions in the human as small as 4 cc. In providing a measure of aerobic and anaerobic metabolism, it is a potentially sensitive research tool for assessing the consequences of coronary artery disease. Similarly, difficulties in the labeling process limit the applicability of radiolabeled platelets and fibrinogen for detecting thrombi. Advances in the development of radioactive tracers that specifically localize in lesions offer future promise for these methods.

Nuclear magnetic resonance imaging is another modality with the potential for estimating blood flow and characterizing tissue and biochemical activities. Current efforts have resulted in very limited success, but research in applying this technique to assessment of peripheral vascular disease is continuing. It is doubtful whether this method can be useful in visualizing coronary arteries because of artery motion and the apparent limitation of resolution to about 3 mm.

There is ongoing research into the application of microwave imaging to biological problems, but no feasibility has yet been demonstrated for its use in the assessment of atherosclerosis. This technique does have the potential for characterizing tissues on the basis of conductivity differences as a function of frequency, but solutions to the technical problems of accomplishing this noninvasively are not yet apparent.

Preliminary evidence regarding the performance of ultrasonic and intravenous radiographic techniques is encouraging and challenges us with the question of validation. Validation must not be limited to testing the accuracy of measurements but must also include testing of reproducibility of image generation and interpretation. In vivo comparison of ultrasound with conventional angiographic methods is confounded by the well-known inconsistencies and inaccuracies that occur with subjective interpretations of angiograms. Carefully controlled studies must include pathologic data from surgical and autopsy specimens in animals and humans. These studies must ensure that the pathologic techniques are well defined in terms of preparation of samples. The increasing clinical use of ultrasound imaging, in particular, makes validation of this technique most pressing. As other techniques progress beyond research into the clinical arena, validation with regard to clinical usefulness must be considered.
Noninvasive techniques for assessment of atherosclerosis. Summary of a workshop sponsored by the National Heart, Lung, and Blood Institute, January 1980.

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