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PET scanning

Provides information on function

The acronym PET stands for positron emission tomography. This uses the tomographic principles of radiation detection and subsequent image reconstruction, but it is more than an imaging technique. Positron emission tomography measures local tissue concentrations of radioisotopes in the body and differs from tomographic imaging with techniques such as computed tomography or magnetic resonance imaging in that it provides functional information.

The versatility of this approach is shown by the wide range of variables that have already been measured and potentially can be measured in humans.[1,2] Local tissue perfusion, blood volume, glucose and oxygen consumption, and fractional extractions of various metabolites and substances have all been quantitated and imaged with accuracy. In this, the use of a positron emitting isotope as a tracer is crucial. Radioactive forms of oxygen, nitrogen, and carbon can be made and substituted for the same stable elements in the molecules to be studied, thus avoiding alterations of the normal metabolic rate after introduction into the body that may result from the use of "foreign" isotopes such as iodine or technetium. The activity passing through a volume of scanned tissue can then be measured.

The variety of functions that can be assessed and imaged is limited by the availability of tracers that can be rapidly labelled chemically with the isotopes, which have extremely short half lives (for example, the half life of oxygen-15 is 2·1 minutes and that of carbon-11, 20 minutes). Measuring the amount of a labelled molecule in the tissues depends on several chemical, physical, and biological factors, any of which may be the focus of primary, clinical, or biological interest. The development of new PET tracer techniques depends on isolating this focus.

Measuring the oxygen and glucose metabolism has been widely used to investigate cerebral function and disease during the 10 years that PET has been used in humans. The brain uses these substrates as the sole providers of metabolic energy, and hence the consumption of glucose or oxygen, or both, reflects total neuronal function. Techniques have been used to highlight areas of the brain that participate specifically in performing motor, verbal, visual, and other tasks.[3] As the methods have become more complex so rapid measurements, which can be repeated at the same session, are now possible, permitting complex analyses of neuropsychological functions and of responses to external stimuli.[4] Metabolic measurements are also valuable in delineating areas of the brain with disturbed function—for example, the abnormalities of parietal and posterior temporal metabolism described in patients with early Alzheimer's disease.[5] Another example is identifying subjects at risk of Huntington's disease by finding low energy metabolism in the caudate nucleus. This pattern is universal in the established disease and its finding in apparently healthy people has raised the possibility of presymptomatic identification of gene carriers.[6] Conversely, raised metabolism is found during pathological excitation, such as in epilepsy. PET has been found clinically useful in assessing patients with partial complex epilepsy for treatment with temporal lobectomy by detecting hypometabolic areas in a temporal lobe during the interictal period.[7-9]

Measuring haemodynamic variables such as tissue perfusion and blood volume together with oxygen metabolism has helped our understanding of ischaemic and pre-ischaemic states[10-12] and is being developed further for evaluating haemodynamic compromise in patients with stenotic and occlusive disease of arteries in the neck. This ability to measure and image hypoxia and ischaemia is also proving useful in studying myocardial ischaemia[13] and the local physiology of tumours of the brain and other organs.[14,15] More recently, methods have been introduced to measure the function of neurotransmitter systems in Parkinson's disease,[16-18] schizophrenia,[19-21] and partial complex epilepsy.[22,23] Other tracers are being developed for the serotonergic system.[24-28] In a few cases tracers have already been used for imaging and measuring the function of both presynaptic and postsynaptic components of a neurochemically distinct pathway.

The scope for labelling a wide range of chemicals and pharmaceuticals is immense. Recent advances suggest that further tracers will be identified and new methods developed in the coming years, while the performance of the PET scanners will probably also improve. The combination of metabolic and transmitter specific tracers is particularly attractive for investigating neurological disease, particularly the degenerative disorders of the deeper cerebral structures. The prospect of being able to classify in life some degenerative diseases presenting as dementias or akinetic-rigid syndromes will allow us to study their natural course and possible treatments.[29] Other applications are likely in oncology,[30] cardiology, and local blood-brain barrier function.[31,32]

PET is a general technique which may be applied to any part of the body. Apart from metabolic and transmitter studies it may be used to measure tissue concentrations of any labelled substance or drug and its rate of change with time.[33] Nevertheless, its clinical utility is frequently questioned. Certainly, the technique is difficult (because of the short lived isotopes), expensive on capital costs, (necessitating a cyclotron, PET scanner, hot cells, and computing facilities), and

demands multidisciplinary teams with considerable skills to carry out and, above all, interpret the tomograms. Nevertheless, experience from over 50 centres in the world has shown that this essentially non-invasive technique can provide unique quantitative functional information and that it is an important addition to our understanding of the pathogenesis and evolution of human disease.

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Regular Review

Treating mild hypertension

Agreement from the large trials

Report of the British Hypertension Society working party

It is now generally accepted that treating moderate or severe hypertension improves the prognosis. With malignant hypertension the improvement was sufficiently clear for historical comparisons to justify active treatment,[1-5] and benefit in more moderate but still severe hypertension was shown in small studies of simple design.[6 7] Although the risks of milder hypertension have been shown,[8] the value of treating those without evidence of damage to end organs such as the heart, kidney, and eye has until recently remained untested. Many large, carefully designed studies were, however, started in the 1970s to test the value of treatment (table I).

The last of these studies was reported in 1987,[20] and no major prospective trial remains to be reported in the immediate future. The British Hypertension Society accordingly set up a working party to establish how far it is possible to give firm advice about treating patients with mild hypertension. Although reached independently, our conclusions are broadly consistent with those reached by a recent joint conference organised by the World Health Organisation and the International Society of Hypertension.[21]

The large scale trials have used fundamentally different control groups. Some have employed placebo[9-11 13-15] or untreated [12 16] controls; others have compared two forms of treatment. In two trials regimens based on β blockers have been compared with regimens that have specifically excluded β blockers.[19 20] In addition, the Medical Research Council study allocated patients in the treatment group to regimens based upon bendrofluazide or propranolol.[15] These three last studies therefore deal with the question of possible specific benefit from β blockers. Two United States trials compared multiple interventions carried out by specialist physicians with usual ("referred") care.[17 18] The absence of an untreated control group in these studies reduces their relevance in assessing the value of treatment. The design of these trials and a summary of the main results are presented in tables I and II.

The effect of antihypertensive treatment (as opposed to multifactorial treatments) may be assessed only from trials that included an untreated or placebo treated control group. There are appreciable differences in the incidence of end points (such as deaths or cardiovascular events) among these