D. Balériaux[1])

Neuroradiology: past, present and future

One of the earliest radiographs ever made was of the human skull, and by 1896 radiology had proved itself in localizing bullets in the skull and cervical spine[1,2]. Plain skull radiographs were of immense value in detecting trauma and the presence of foreign bodies, but imaging of the brain itself presented a seemingly insuperable problem: the problem of visualizing the radiolucent soft tissue of the brain within the virtually radiopaque box of the skull. In spite of the rapid advances in X-ray imaging technology, it was to be nearly 70 years before a satisfactory solution was found, allowing pathological changes to be visualized in the tissue of the brain itself.

Indirect signs

The earliest methods used for the detection of brain tumours depended on indirect signs. For example, as the pineal gland is normally calcified, it shows up on the X-ray image, marking the midline of the brain. A shift in its position indicates the presence of a space-occupying lesion. Infrequently, the tumour itself might also be calcified, allowing it to be observed directly (Fig. 1).

Other indirect signs were used for detecting intracranial hypertension. These included thinning of the sella and, in children, digital impressions on the inside of the skull and opening of the cranial sutures, due to expansion of the brain.

Early detection of hypertension is important, as it allows appropriate measures to be taken to avoid neurological deterioration in children, while relief of hypertension in adults can sometimes restore demented patients to normal within a few days.

Indirect signs continued to play an important role in cranial diagnostics until well into the 1960's.

Contrast media

Direct techniques for visualizing elements of the brain, such as the ventricles and the blood vessels, as well as the spinal cord, depended on the use of contrast media.

As described by Dr O. Wayne Houser in his President's Address at the 1994 RSNA[3], the identification of suitable contrast media for use in neuroradiology was, to a certain extent, the recognition of the value of chance findings.

The first technique to appear was the use of air for visualizing the outline of the brain and the ventricular system (Fig. 2a), closely followed by direct injection of contrast media into the cerebral ventricles (Fig. 2b).

The former technique, first presented by Dandy in 1918[4], remained in general use until the mid 1970's. It depended on the fact that air was much less absorbent to X-rays than the liquor normally present within the ventricles. It did not really show the brain itself, but only spaces within and around the brain. Nevertheless, compression or displacement of the ventricles was a useful indirect sign of the presence of a tumour.

Although air was also used for delineation of the spinal cord (Fig. 4), it was quickly superseded by the use of positive contrast media, such as iodized oil or iophendylate (Pantopaque). This was the result of an accidental discovery by Sicard and Forestier, who observed the flow of oil into the thecal sac following an injection into the lumbar musculature[5].

Another important development was the introduction of cerebral angiography, first applied in vivo by Egas Moniz, who injected sodium iodide directly into the carotid artery[6]. Subsequently he was to use thorium dioxide[7], which gave excellent short-term results, but proved to have long-term toxicity. In order to capture the rapid flow of contrast medium through the cerebral arteries, Moniz mounted his films on a turntable, operating on the principle of a revolver. Later, multiple exposures were obtained using the Elema Schönander AOT film changer.

1) Department of Neuroradiology, Hôpital Erasme, Brussels, Belgium.

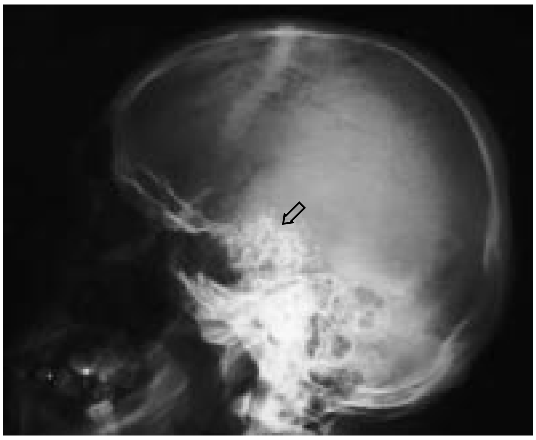

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Fig. 1. Plain skull radiograph showing a calcified tumour in the sellar region (arrow).

2a

2b

Fig. 2. Contrast techniques.
a. *Pneumoencephalography: midline tomography showing the fourth ventricle.*
b. *Iodoventriculography.*

There are two principal applications for cerebral angiography. The first is the detection of lesions or abnormalities in the arteries themselves, such as occlusions, aneurysms or arteriovenous malformations (AVM's). This has always been the most important application, but the advent of new imaging modalities has resulted in a significant reduction in the total number of cerebral angiographies performed.

The second application is the detection of tumours by observing displacement of the vessels or neovascularization. Neuroradiologists rapidly learned to recognize the characteristic patterns of the arteries and veins, and to detect any abnormalities which could indicate the presence of a lesion. This is gradually becoming a lost art.

Tomography and subtraction

The use of air and positive contrast media showed structures that were previously invisible, but they did not always show them very clearly. The faint images of the structures under examination were often obscured by the overlying bones of the skull and spinal column.

Two ingenious solutions to this problem were suggested by B.G. Ziedses des Plantes in his doctoral thesis *Planigraphy and Subtraction: Roentgenographic Differentiation Methods,* published in 1934[8].

Tomography

Planigraphy, later to be known as tomography, was a form of body section imaging in which the imaging assembly was moved around a fixed point in the body. Structures lying in the same plane as the rotation point would be imaged relatively clearly, while structures lying above or below the plane would be blurred. Ziedses des Plantes claimed to have got the idea from looking into a glass of beer. The technique provided clearer images of the skull base than any previous method (Fig. 5).

Ziedses des Plantes' Planigraph was taken into commercial production by Massiot of France, now part of Philips Medical Systems, and eventually became the Philips Polytome, which set the standard in tomography until the advent of computed tomography (CT) in the 1970's.

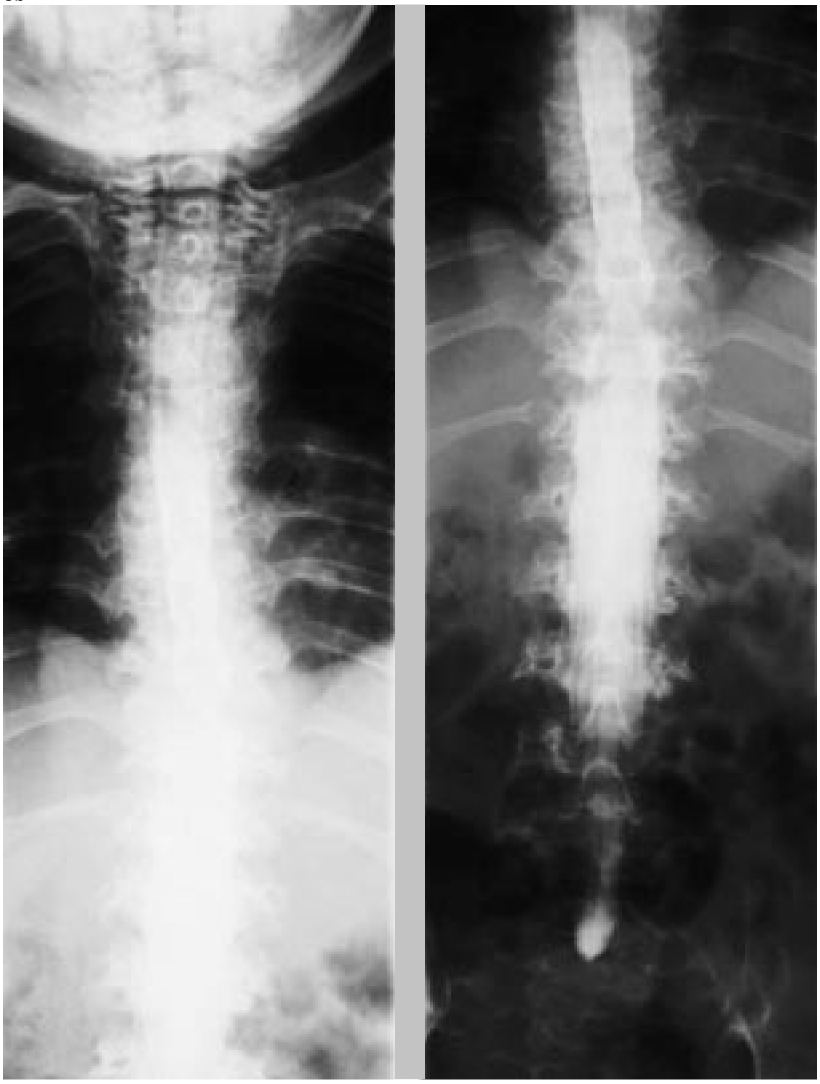
Fig. 3. Myelography.
a. *Introduction of contrast medium.*
b,c,d. *Myelograms. The patient is an achondroplastic dwarf.*

Fig. 4. Sagittal tomography in air myelography.

Fig. 5. Large, partially calcified chondromyxoid tumour of the skull base.
a. *Plain radiograph.*
b,c. *Two tomographic exposures from a series of layers, showing the calcified tumour in more detail.*

3a

3b



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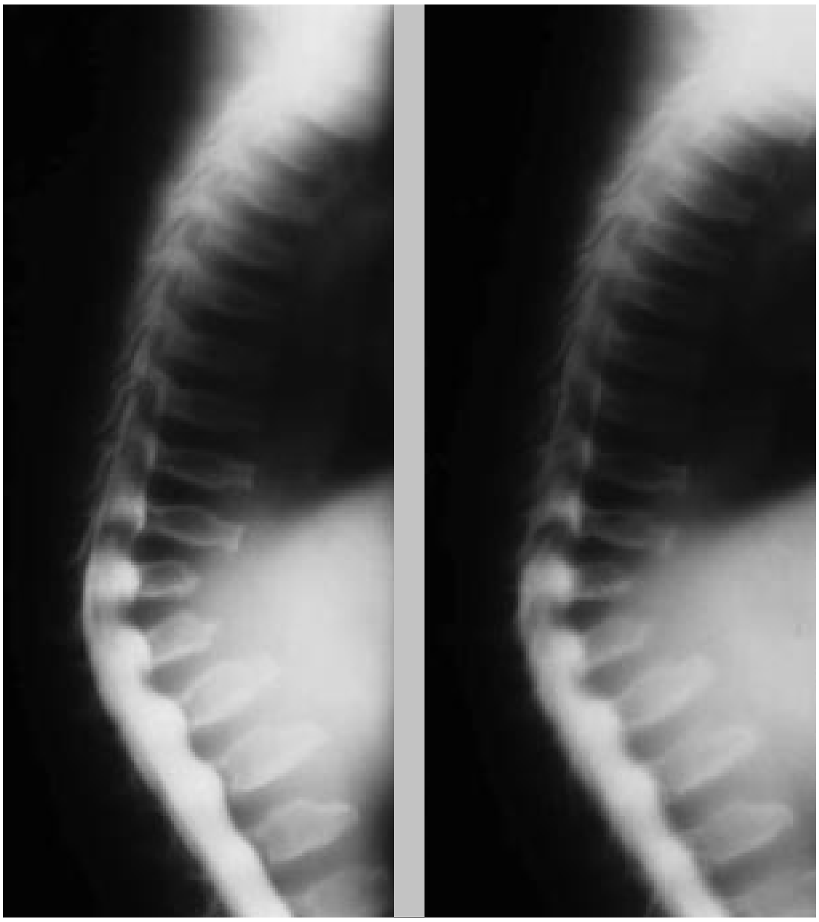

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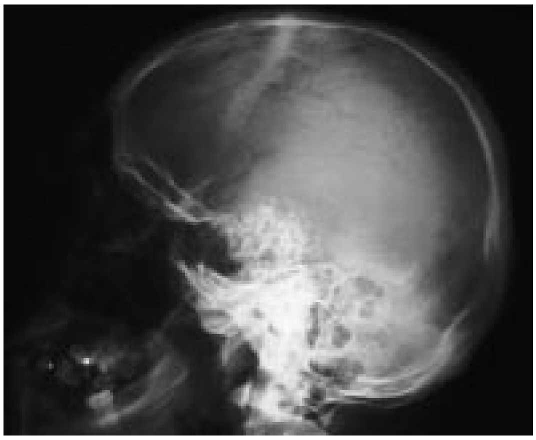

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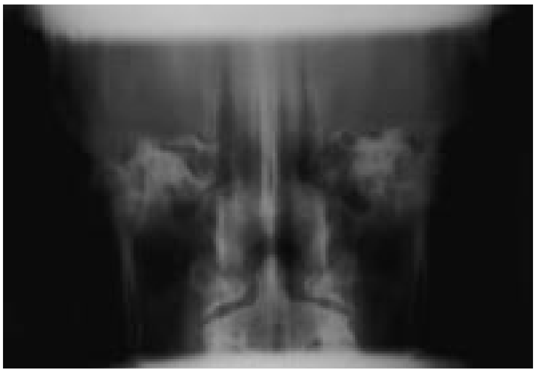
Fig. 6. Linear tomography.

Fig. 7. Pluridirectional tomography.



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Tomography was used to visualize the structures of the skull and brain layer-by-layer. Linear tomography gave acceptable images (Fig. 6), but a pluridirectional movement such as that of the Polytome gave better results (Fig. 7).

Subtraction

Subtraction was based on the principle of subtracting one radiograph from another so that only the differences between them remained. Its principal application was in angiography but, although the principle had been described in detail in Ziedses des Plantes' thesis in 1934, it remained little known until Ziedses des Plantes published a monograph on the subject in 1960. By that time, the importance of angiography had become more widely recognized, and subtraction angiography soon became an established technique.

Originally, subtraction was performed photographically (Fig. 8a) but by the end of the 1960's various television-based systems had become available. In our hospital, we used such a system (Evaluscope, Siemens) throughout the 1970's.

With the advent of digital techniques in the early 1980's, subtraction became generally available in the form of Digital Subtraction Angiography (DSA) (Fig. 8b,c).

Somersaulting

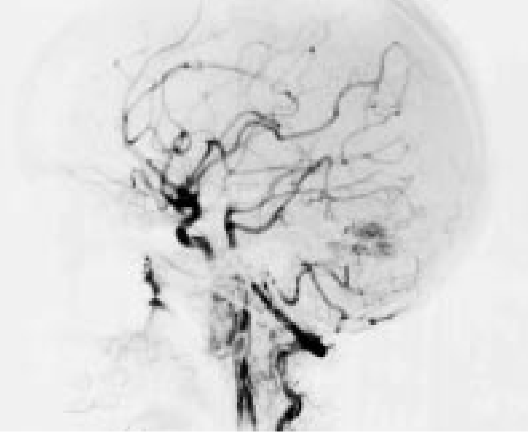
In the 1960's, the standard imaging equipment for neuroradiology was a tomograph with an isocentric chair.

The isocentric chair allowed the patient to be rotated in a somersaulting technique, so that the whole of the cerebral ventricles could be visualized step-by-step using a relatively small amount of air or gas. This fractionated technique was less stressful for the patient than using a larger amount of air to displace all of the fluid in the ventricles, but it remained uncomfortable and dangerous. In our hospital we used the Mimer chair, which could convert from a bed, and served as a patient support for tomography.

The examination was routinely preceded by assessing the intracranial pressure via the optic fundus examination. Hypertension was always a contraindication, as excessive pressure could cause explosive decompression via the lumbar puncture, causing the amygdala to constrict the medulla oblongata, resulting in the death of the patient. If hypertension was detected, we would perform ventriculography with an oil- or water-soluble contrast medium, introduced directly via a burrhole in the skull (Fig. 2b).

Pneumoencephalography was performed on a regular basis. We were fortunate in having the excellent atlas published by Dr G. Ruggiero, an internationally acknowledged expert[9]. The examination was always performed under general anaesthesia, using NO + O_2 rather than air, as this reduced the subsequent pain and nausea. Multiple tomography was performed with the Mimer chair and a cassette with a stack of four or five films (Fig. 2a).

We used both gas cisternography and oil cisternography. If a tumour of the hypophysis was suspected, gas was injected by the lumbar route into the perisellar cisternae. The gas then



8a

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8c

Fig. 8. Subtraction angiography.
a. *Photographic subtraction.*
b. *DSA image before subtraction.*
c. *DSA image after subtraction.*

surrounded the suprasellar cisternae and outlined the tumour.

In the case of a suspected acusticus neurinoma, we would try to introduce gas into the internal auditory canal. If the acusticus neurinoma was relatively small, so that it did not impede the passage of the gas, this approach was generally successful. If not, we would follow it up with an oil injection.

Nuclear medicine

The isotope scanner also came into widespread use in the mid 1960's. As it was based on the uptake of labelled isotopes, it gave some indication of the brain metabolism, while tumours might also show up as regions of increased activity.

In 1964, Di Chiro[10] noted that intrathecal isotope injection could show the CSF flow dynamics. This was an important step forward, as anomalies in the flow dynamics can cause brain dysfunction.

Initially, images of isotope uptake were obtained by rectilinear scanners, in which the patient was scanned in parallel lines by a motorized detector. However, in 1963 Kuhl and Edwards[11] published details of a technique using a computer, coupled with a transverse section imaging device, to produce transaxial tomograms of the head using single gamma ray radionuclides. This technique later became known as single photon emission tomography (SPECT).

By 1971 Kuhl and Sanders[12] were using transverse section isotope scanning for the differential diagnosis of brain lesions.

Transverse sectional imaging yielded a wealth of information, but its value was limited by poor spatial resolution and its dependence on isotope uptake (Fig. 9).

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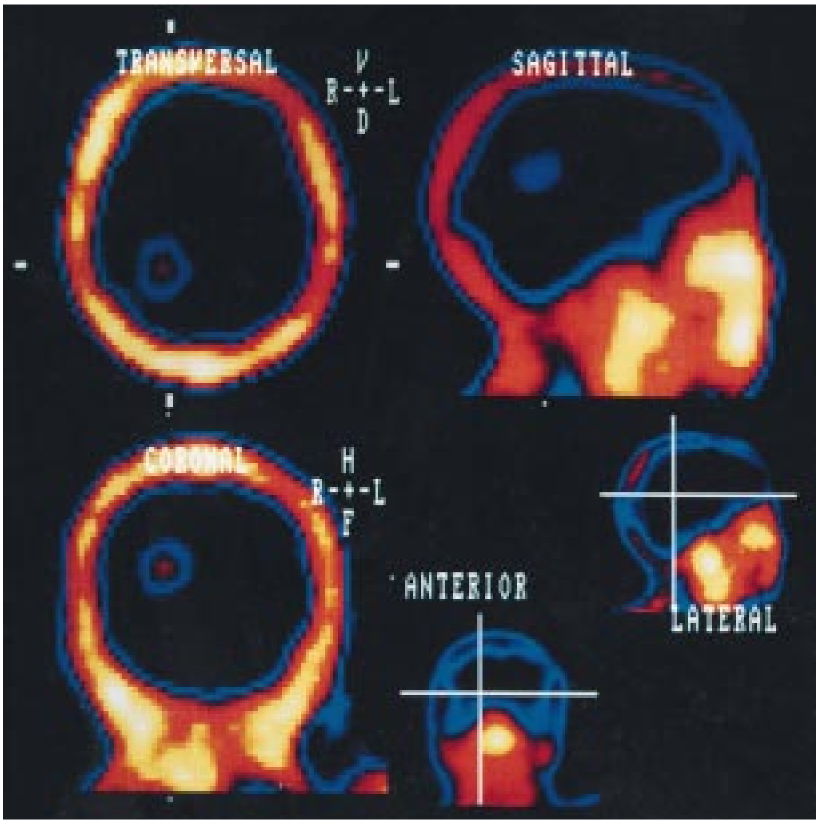
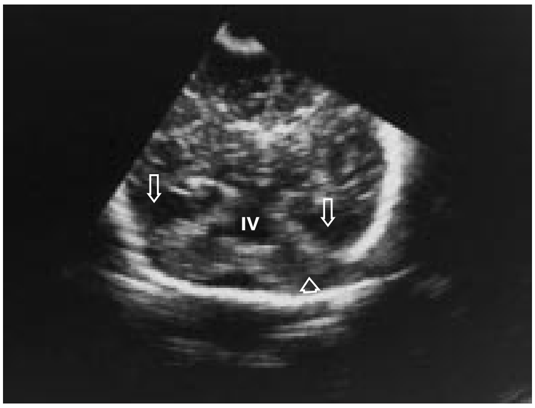


Fig. 9. Radioisotope imaging.

Fig. 10. Echography of the brain. Images reproduced by courtesy of Professor E.F. Avni.
a. *7 day old baby. Coronal view showing fourth ventricle, temporal lobes and posterior fossa. The hyperechoic white areas are blood, indicating a subarachnoid temporal haemorrhage.*
b. *Fetal head (same patient as* **a***). Parasagittal view showing fourth ventricle and cerebellum.*
c. *Head of 15 day old baby. Coronal view showing enlarged fourth ventricle.*
d. *Head of 15 day old baby (same patient as c). Parasagittal view showing enlarged fourth ventricle and cerebellum.*



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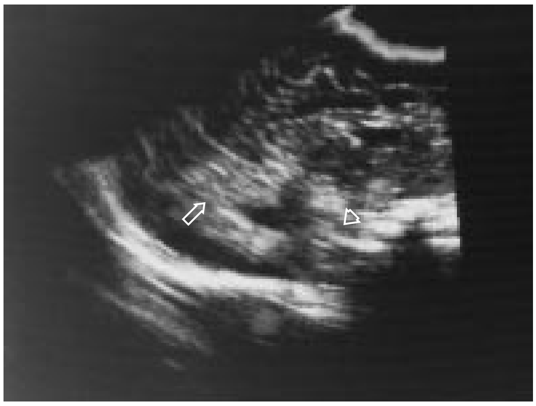

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Ultrasound

In the early 1970's, there was a growing interest in ultrasound. Its non-invasive nature made it particularly attractive for paediatric applications, especially in follow-up studies where repeated exposure to X-rays would not be justified.

Ultrasound was of value in detecting fetal abnormalities and for detecting anoxic lesions in neonates and young children (Fig. 10). A- and B-mode echoencephalography could be helpful in the diagnosis of hydrocephalus, and pulsatile echoencephalography yielded characteristic results in various diseases.

The whole neonatal ventricular system could be visualized using the fontanelle as an acoustic window.

A-scan echoencephalography was also used in the mid 1970's for determination of midline shift in both children and adults. Although this technique avoided X-ray exposure, it was not very accurate, and was rapidly superseded by the advent of computed tomography (CT).

In the late 1980's, Levine used a duplex Doppler technique for cerebrovascular mapping in babies. Transosseous ultrasound could be used for the detection of ischaemia, and for monitoring subarachnoid haemorrhage.

Computed tomography (CT)

In 1972, the whole discipline of neuroradiology was revolutionized by the introduction of the

CT scanner, developed by Godfrey N. Hounsfield at EMI Ltd. Hounsfield noted that conventional X-ray techniques could not distinguish between different tissues, as they only recorded the mean absorption of all the tissues through which the X-ray had penetrated. He reasoned that a system which performed sets of X-ray measurements through the body at a multitude of different angles would make more efficient use of the information that the X-rays could give, and might make it possible to distinguish between the various tissues of the body[13].

The original laboratory model used a gamma-ray source, and had an acquisition time of nine days, with a reconstruction time of $2^{1}/_{2}$ hours. Nevertheless, the system worked, showing that the principle was sound.

A clinical prototype was built by EMI, and installed in Atkinson Morley's Hospital, London, in 1972. The first patient scanned had a suspected brain lesion, and the image clearly showed a circular cyst in the brain, demonstrating that the machine was sensitive enough to distinguish between normal and diseased tissue.

In 1979, Hounsfield was awarded the Nobel Prize in Medicine for his work on CT, together with Allan Mc Cormack who had independently investigated the mathematical basis of CT reconstruction. In addition to many awards, Hounsfield received a knighthood in 1981.

The EMI scanner made it possible, for the first time, to obtain direct images of the soft tissues of the brain. Primary tumours and metastases, their origins, infiltrations and their blood supply could all be seen in detail. At a stroke, plain skull radiography, ventriculography, pneumoencephalography and much of nuclear medicine had been superseded.

We decided to buy a whole-body CT scanner, and in 1976 a Delta Scanner (Ohio Nuclear) was installed in our department. An unusual feature of this system was its ability to provide images in colour. The image reconstruction software had originally been devised for applications in astronomy and satellite research, and had provision for false colour (Fig. 11). Although the images were undoubtedly of artistic merit, the arbitrary allocation of borderlines in graduated areas made little contribution to the diagnostic effectiveness. History repeated itself some years later in the introduction of MR imaging (Fig. 12).

The Delta Scanner was painfully slow by present-day standards, taking $2^{1}/_{2}$ minutes for simultaneous acquisition of two slices, and the slice thickness was 1 cm. Nevertheless, it was an almost incredible improvement on previous

11a

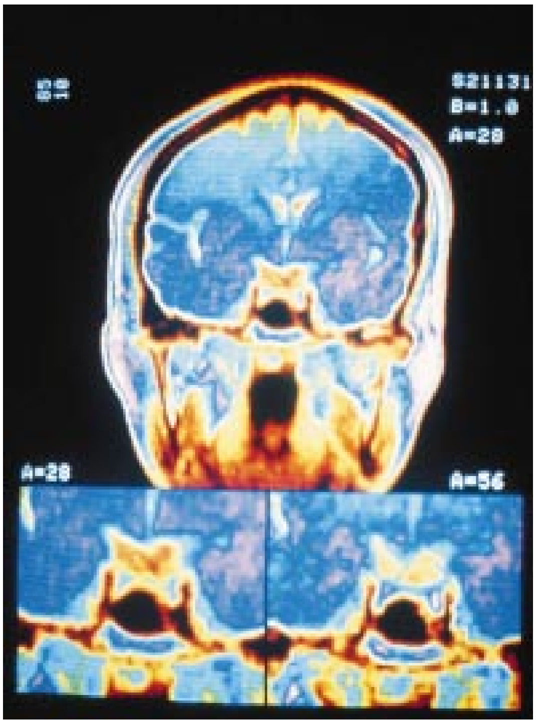

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Fig. 11. Early CT image with false colour.
a. *Axial head scan.*
b. *Enlarged detail.*

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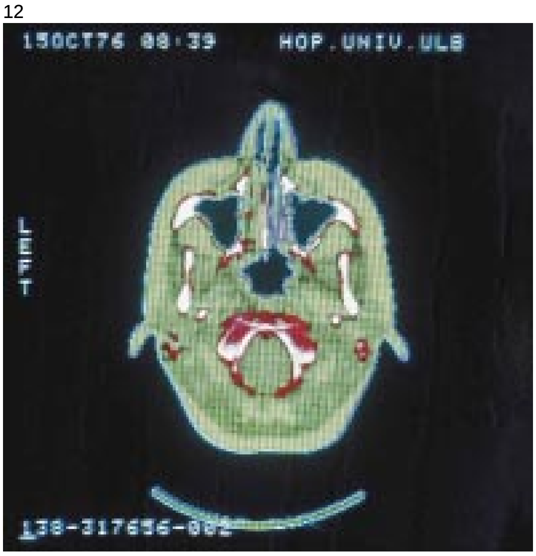
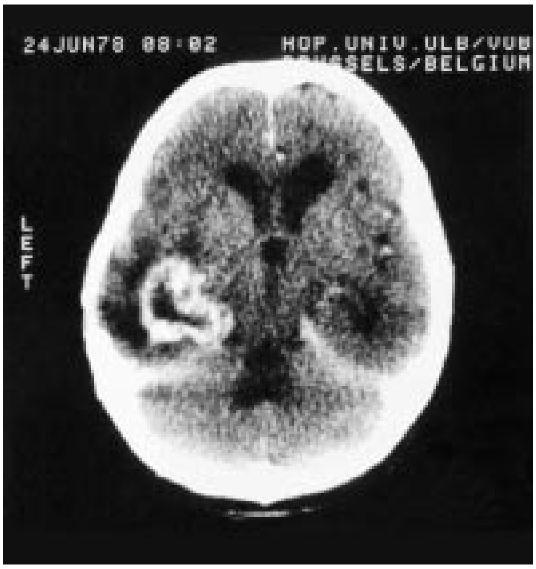


Fig. 12. Early MR image with false colour.

Fig. 13. Early CT images. Although the quality is poor by present-day standards, the image clearly shows the ventricles, and also allows discrimination of normal and pathological soft tissues, representing a considerable improvement over gas or contrast cisternography.

Fig. 14. The effect of contrast medium in CT.
a. *Plain image.*
b. *Image following injection of contrast medium.*



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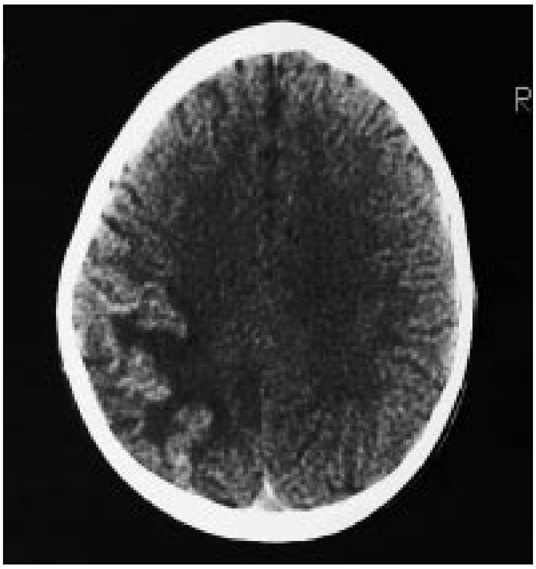

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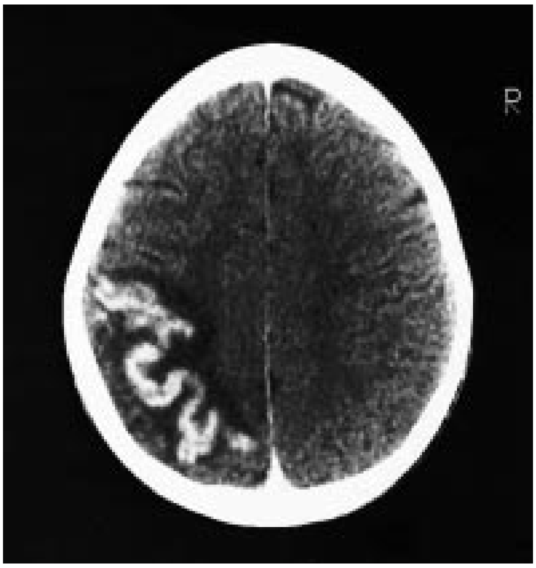


14b

techniques. We could not only see the displacement of the ventricles very clearly, but we could also see the exact location and extent of the tumours themselves (Fig. 13). Careful selection of the grey scale and window levels allowed us to take the first tentative steps in soft tissue discrimination. Although the native CT images yielded far more information than earlier methods, it was soon found that even better results could be obtained with the use of contrast medium (Fig. 14).

The first CT scanners had no provision for scout views, so that it was not always easy to recognize the exact level in the body. Our approach to this problem was the use of a set of radio-opaque rods of different lengths. The number of rods in the image gave a guide to the slice position: the fewer the number of rods, the more distal the slice (Fig. 15).

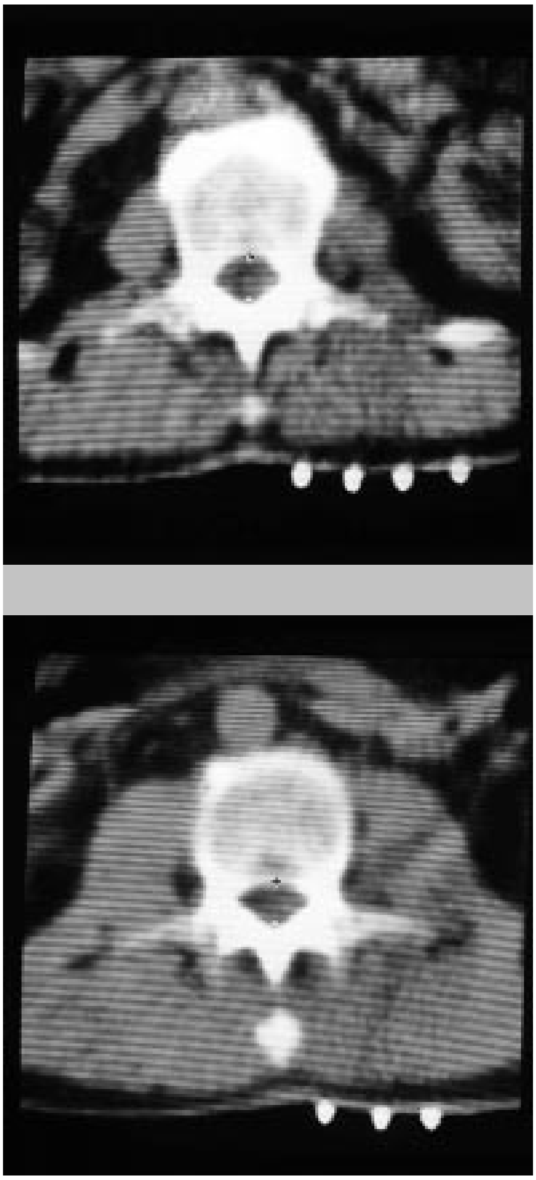
By 1981, we had a CT scanner (Somatom, Siemens) providing thin slices that could be stacked for three-dimensional reconstruction (Fig. 16). Since then, computerized image processing has given virtually unlimited scope for CT angiography, reformatting in any selected plane, and three-dimensional images giving a surgeon's eye view of pathologies.

Digital subtraction angiography

The basic principles of subtraction had been described by Ziedses des Plantes in 1934[8], but the technique was not generally applied until the 1960's, when interest was reawakened by the growing importance of angiography. The original photographic subtraction technique yielded relatively good results (Fig. 8a), but was time-consuming and cumbersome.

By the end of the 1960's, various television-based systems for subtraction had become available, and we used such a system (Evaluscope, Siemens) throughout the 1970's. However, this system depended on the availability of images on film.

Although the use of a balloon for occlusion of the cerebral vessels and carotid arteries had been pioneered by Serbinenko in the late 1960's, and was described in the literature in 1971[14,15], the absence of a satisfactory method for real-time angiography prevented widespread application of transluminal interventional procedures.



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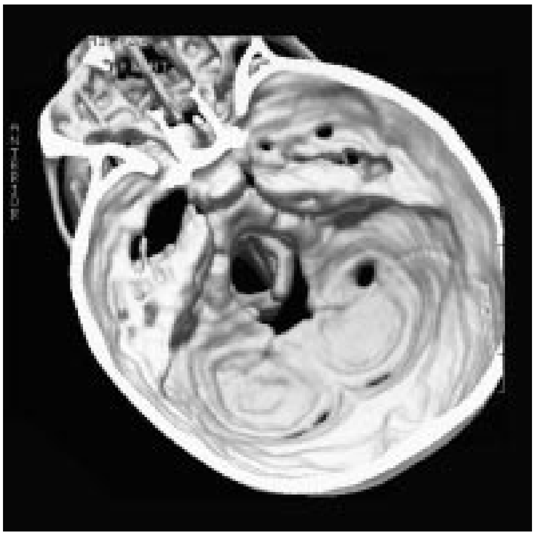

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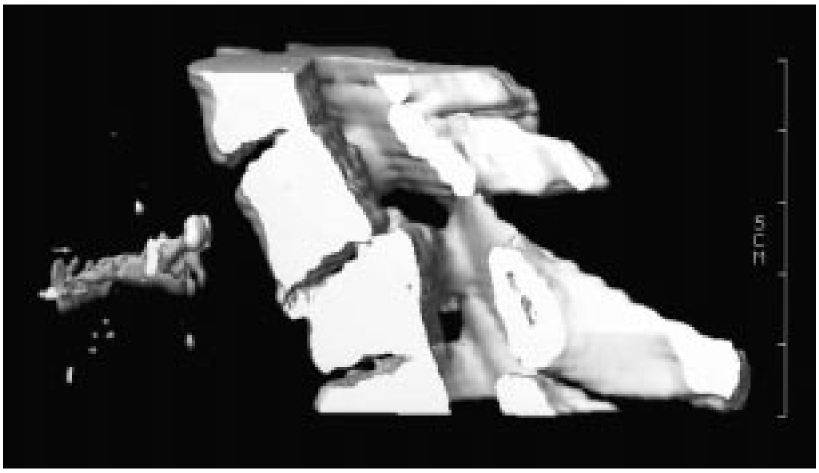

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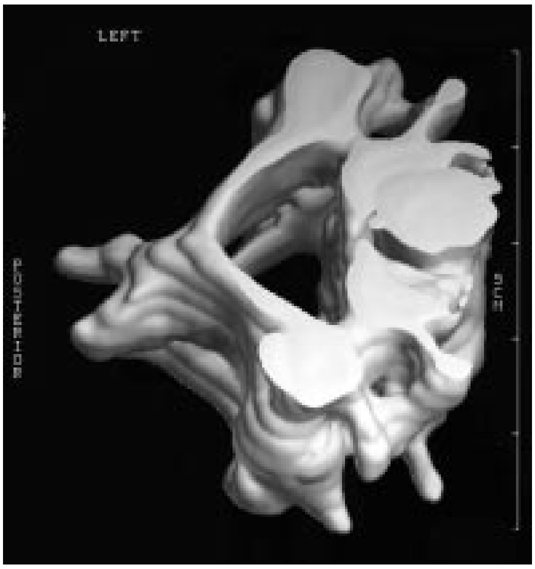

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Fig. 15. Early CT systems had no provision for scout views. Radio-opaque rods of different lengths give a guide to the slice position. The fewer the number of rods, the more distal the slice.

Fig. 16. By 1981, thin slices could be stacked for three-dimensional reconstruction.
a. *Reconstruction of the skull of a child, less than one year old, showing bone deficit associated with a large meningocele in the skull base.*
b. *Compression fracture of C7 and luxation of C6-C7 with constriction of the vertebral canal.*
c. *Reconstruction of a vertebra following an anterior cervical graft, showing an unobstructed vertebral canal.*

With the advent of digital techniques in the early 1980's, subtraction became generally available in the form of Digital Subtraction Angiography (DSA) (Fig. 8b,c). This technique, originally referred to as 'computerized fluoroscopy', was developed by

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Fig. 17. Prototype MR installation at the Philips Medical Systems factory in Best, the Netherlands (author's photograph).

Fig. 18. Modern MR images.

Charles Mistretta and Andrew Crummy at the University of Wisconsin[16].

DSA provided real-time digital processing without intermediate analogue storage, making it possible to view fully processed and enhanced subtraction angiograms while the contrast material is flowing through the region of interest. As a result, real-time angiograms both with and without subtraction are now available for rapid acquisition of diagnostic information, and for an ever-increasing number of interventional applications including balloon angioplasty, thrombolysis, and embolization with coils[17].

Magnetic resonance imaging (MRI)

At about the same time that we purchased our first CT scanner, the first steps were taken in the development of MR imaging systems. Initially, the technique was referred to as Nuclear Magnetic Resonance, as it depended on the properties of the atomic nucleus, but the term 'nuclear' was soon dropped, as patients were sometimes worried by the incorrect but understandable association with radioactivity.

We were fortunate enough to be involved in the development of the first commercial systems, as we had been invited to co-operate with Philips Medical Systems in the development of the Gyroscan range. In this way, our clinical requirements could be incorporated right from the start.

It soon became clear that magnetic resonance offered some very specific advantages. It was non-invasive, and had an unprecedented sensitivity to differences in tissue: the white and grey matter were more clearly distinguished, and

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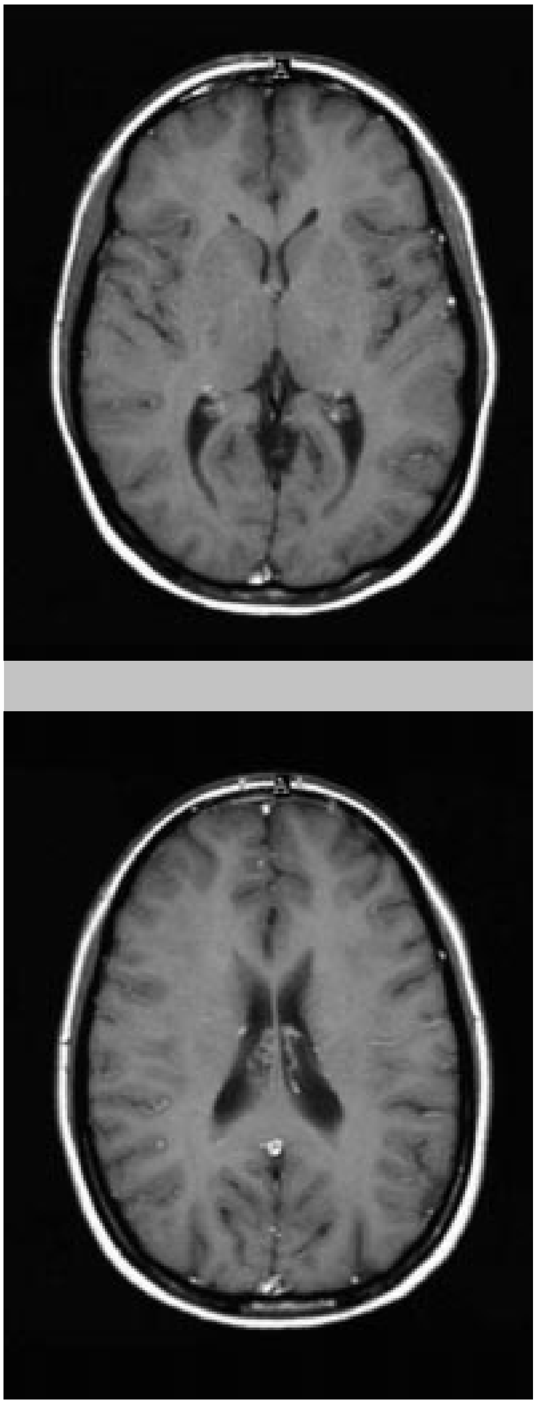

some pulse sequences revealed pathologies that could not be seen in CT or with the standard MR pulse sequences. Moreover, there was a completely free choice of image plane, including excellent midsagittal slices, with no need for reformatting.

The results obtained even with the first experimental system were so good that we were soon bringing doubtful cases to the Philips Medical Systems factory in Best, the Netherlands, which is about $1^1/_2$ hours' drive from our hospital in Brussels (Fig. 17). These were mainly patients with a suspected brain tumour which did not show up on CT.

The procedure was somewhat irregular, and generally involved the author driving patients to the factory in her own car, as there was no administrative provision for referring and transporting patients to a factory. However, the results obtained more than justified the logistic problems, and the patients were more than happy to co-operate. Informed consent was not just a formality.

Modern MR techniques (Fig. 18) are about 100 times more sensitive than CT with respect to tissue discrimination, and are very fast, with the possibility of performing a complete examination in about four minutes. Proton density weighting provides excellent visualization of MS plaques, which can barely be detected on the CT images. Appropriate choice of pulse sequences can also show many brain metastases which are not visible on CT.

Nowadays, no complex neurosurgical procedures are performed in our hospital without prior MR examination. Patients are always screened for brain metastases before resection of primary tumours, e.g. in the lung.

The specificity and sensitivity of MR examinations can be enhanced still further with the use of gadolinium contrast medium. This can give valuable additional information on the possible histology of a lesion, and some lesions only appear after contrast enhancement.

Examinations of the hypophysis show tumours better than repeated CT examinations, particularly as the hypophysis is too close to the skull base for satisfactory CT imaging. Moreover, MR involves no radiation dose, which is particularly important in this type of examination in view of the possibility of excessive exposure of the eyes.

The high sensitivity and lack of radiation of MR examinations is of great value in paediatric applications. The possibility of following brain maturation is of particular interest. Myelinization starts just before birth, and continues very actively through the first two years of life. A sequence of different changes can be seen from month to month.

MR angiography (Fig. 19) is relatively easy, given a little experience and practice. Phase contrast angiograms can be performed in about 20 seconds, with no need for contrast injections, puncture or catheterization. As a consequence, the importance of conventional angiography has declined somewhat, as it is now restricted to the diagnosis of strictly vascular lesions, rather than serving as an indirect sign of the presence of a tumour.

MR spectroscopy has been performed in our hospital on an experimental basis since 1985, under the direction of Professor Segebarth. The main objective is to detect spectral changes in brain tumours due to changes in the proportions of the various metabolites and, if possible, to evaluate the possibility of using them as a basis for differential diagnosis. Some clinics demand spectroscopy before surgery, but we find it less specific than we would like. However, it is certainly useful for the detection of very early anoxic lesions, and for early detection of metabolic changes.

Abnormal metabolite levels could be a possible early sign of Alzheimer's disease. There has been ongoing research into finding a specific MR sign for Alzheimer's disease since 1985, notably that carried out by Dr Brian Ross and his colleagues[18].

The future

Speculation about the future is always dangerous. Sooner or later one's forecasts will always be compared with the reality, and all too often there is something totally unexpected lurking just around the corner. It would therefore be absurd to even try to speculate on the whole of the next century of diagnostic imaging. Nevertheless, extrapolation from current trends generally gives some idea of developments in the short term.

It is virtually certain that the trend towards combined diagnosis and treatment will continue, with increasingly sophisticated interventional procedures for the treatment of aneurysms, arteriovenous malformations and/or stenoses.

Interventional techniques have been in use for a quarter of a century[14,15], but have developed relatively slowly. For example, coil embolization is still being evaluated. On the other hand, endovascular treatment of arteriovenous malformations is now a well-established alternative to surgery or, in some cases, the only available technique. We can confidently predict increasing application of balloon angioplasty, stenting and related techniques in the near future.

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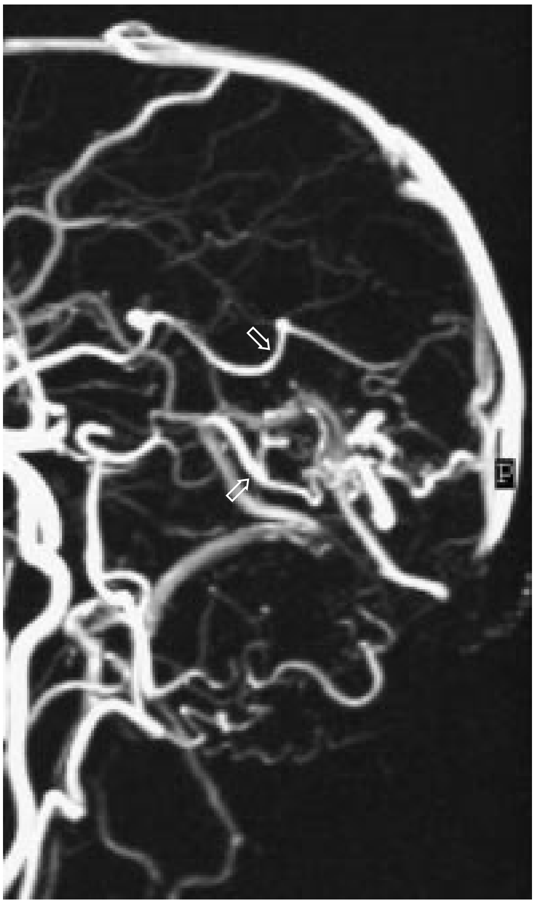

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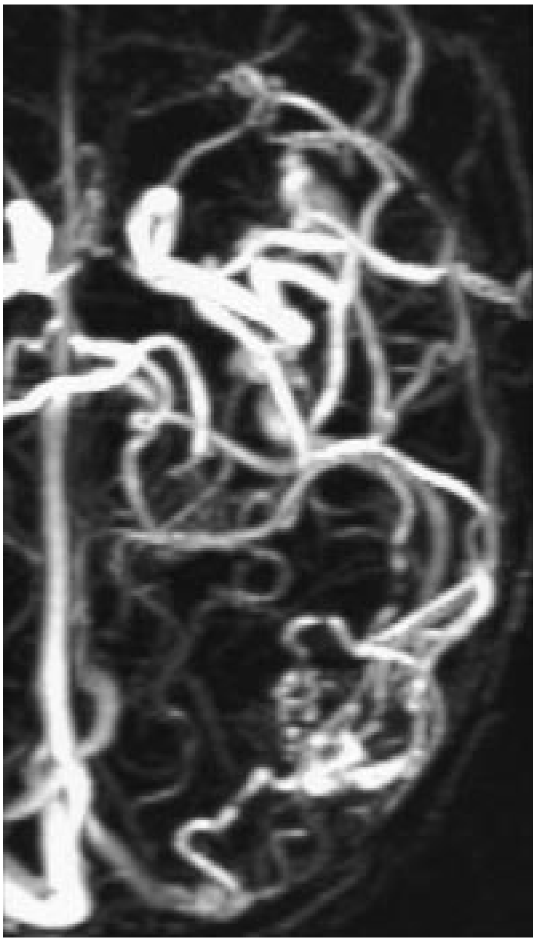

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Fig. 19. MR angiography.
a. *Circle of Willis.*
b. *AVM. High-velocity flow-encoded image showing feeding arteries (arrows).*
c. *AVM. Low-velocity flow-encoded image showing venous drainage (arrows).*
d. *AVM. Low-velocity flow-encoded image. Axial view showing venous drainage.*

There will also be more combinations of imaging modalities (Fig. 20) as well as combinations of imaging and measuring techniques. Combinations of CT or MR with electroencephalography, magnetoencephalography and nuclear medicine will yield new insights into the functions of the living brain, while the combination of MR imaging and MR spectroscopy is already providing additional information on the normal and pathological metabolism.

Proton emission tomography (PET) shows metabolic processes *in vivo*, indicating the sites of brain activity such as response to visual stimuli, as well as memory, which seems to take place in the same sites as the original response. However, PET is inherently slow, whereas MRI can, in principle, provide results in milliseconds.

MR imaging will become increasingly refined. New pulse sequences such as FSE and TSE are continually being developed for faster and better slice acquisition, including simultaneous multiple slice acquisition, while we are now only beginning to appreciate the diagnostic results obtainable with different combinations of pulse sequences. For example, it has long been known that T_1 weighting can give better differentiation of white and grey

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Fig. 20. Combined display. This example combines the bone image from CT and the tumour image from MR.

matter, while T_2 weighting tends to be more sensitive to pathologies. It has also been found that the plaque associated with multiple sclerosis shows up better with ^1H density weighting. Some tumours mimic normal tissue in the more commonly used pulse sequences, but can be revealed by special pulse sequences such as FLAIR. The relationships between pulse sequences and pathologies will undoubtedly be explored further in the coming years.

The combination of MR imaging and spectroscopy and, in particular, new MR procedures for functional brain imaging such as brain activation studies, perfusion imaging and diffusion imaging, coupled with increase dcomputer power, should allow us to watch the brain at work: literally as fast as thought.

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Fig. 21. Combination of an optical 3D localizing system and a digital workstation allows for advanced applications in (neuro)surgery. The example shown is the Philips EasyGuide Neuro.

Current computer techniques provide ever-faster reconstruction, as well as a vast assortment of image processing techniques, including reformatting in curved planes such as the surface of an organ or vessel trajectories. Fast reconstruction in multiple layers offers new diagnostic possibilities, such as cine excursions through the vessels.

It is also possible to combine images from several modalities in a single display (Fig. 20).

Stereotactic procedures with accurate localization using CT, MR and PET images are already being used for precision biopsy procedures and tissue implantation and are also used for micro-interventions (Fig. 21).

Although neuroradiology has been around for a century, the most impressive developments have taken place within the last two decades, and the pace of development is accelerating rapidly. We can therefore confidently predict that, with the probable exception of W.C. Roentgen's original stunning discovery, developments over the coming century will be even more impressive than those of the last hundred years.

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