Wellcome Film Project

Ultrasound in Tumour Diagnosis

The Scientific Basis of Medicine

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<**Opening titles**>

<**Dr VR McCready to camera**>

Today I would like to discuss the use of ultrasound in the detection and differential diagnosis of tumours. Ultrasound is one of several rather new techniques which have the special attraction of finding tumours with minimal trauma to the patient. These new techniques are of most use in and around the abdomen where the conventional x-ray techniques would require an injection of some form of contrast medium. I would like first of all to discuss these new approaches to tumour diagnosis, to indicate their limitations and, incidentally, show where ultrasound fits into the general picture of diagnosis. I would like then to discuss the scientific basis of ultrasound in order to show you its limitations and also its great potential. Following this I would indicate how ultrasound techniques are of especial value to different types of tumour in the various organs. Then my colleague Dr David Cosgrove would like to show you how ultrasound was applied to a particular clinical problem and how it fitted in with the other forms of diagnosis. Finally, a physicist colleague, Dr David Nicholas will demonstrate some of the newer and more exciting methods of trying to tissue type and find tumours and diagnose them more objectively and perhaps, one hopes, making the doctor a little more superfluous.

There are three new main atraumatic ways of diagnosing tumours at the present time.

<**McCready over tables and diagrams comparing three atraumatic methods of tumour diagnosis**>

These include radio isotope techniques, computerised axial tomography using x-rays and then, finally, ultrasound. The isotope techniques involve the use of a detector and injection of a radiopharmaceutical into the patient. Generally, at the present time, the tumours are shown indirectly since the radiopharmaceutical concentrates in normal tissue rather than in the tumour. Because the tumour itself is non-radioactive, this poses basic limitations and we are not able to show very small tumours. There is also not likely to be very much progress in instrumentation involved so we're striving to find other methods of finding tumours such as ultrasound.

The display of tumours using computerised axial tomography and x-rays depends upon the differential absorption of x-rays within the tumour and in normal tissue. In principle, the x-ray tube shines rays through the patient at several different angles and the computer calculates the organs where the beams cross. In practice, the resolution of the device is still behind that of ultrasound although it is still better than that of the isotope techniques. It shows the outlines of the organs very clearly, but so far, in spite of its extreme insensitivity, it does not show tumours within organs as clearly as ultrasound.

Ultrasound techniques also depend upon the absorption of ultrasound within the tumour or the normal tissue, but they also, in addition, depend upon deflexion at interfaces between organs and between the tumour and the tissue. The particular advantage of ultrasound is that radiation is not involved; it has good resolution –

something like 1-2mm at 2,000,000 cycles per second. The resolution is particularly good in depth but also laterally. It is fine, from the patient's point of view, since it doesn't involve any injection and therefore doesn't hurt the patient. Because it is so simple, it is of especial value in screening patients or in making repeated measurements during the progress of a tumour or its regression on treatment.

<**McCready to camera**>

It is worth looking at ultrasound in a little more detail to show the physical basis of the technique, partly to show its limitations but also to show its great potential for the future.

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<**McCready demonstrates an ultrasound transducer to camera**>

Ultrasound is produced by a transducer such as this. This particular one contains a crystal which rings at its own frequency of about 2,000,000 cycles per second when stimulated by a pulse of electricity. The sound waves then go out towards the patient, meet some interface within the patient, are reflected back again, hit the crystal, and this starts it to ring again and this time produces a pulse of electricity which goes through the cable into the receiver and produces some form of display.

Sound waves move through tissue and water at a constant velocity. Unfortunately, sound does not penetrate air to any significant extent and therefore it is difficult to examine structures behind the trachea, within the lungs, or in or around the abdomen if there's gas present. The sound is observed as it travels through the tissue and we use a […]

<**McCready over diagram of ultrasound waves**>

[…] special type of amplifier to amplify those echoes coming from the deep parts of the body. Here's an example in this diagram where the change in amplifier gain is seen on the lower curve; as the sound goes deeper into the body the amplifier increases its gain and the end result is a set of amplitudes of equal height although, in fact, the sound is being absorbed as it goes through the tissue.

<**McCready to camera**>

High frequency sound waves have better resolution because the curves are closer together. We tend to use high frequency work of transducers in ophthalmic situations when we don't want to see any great depth but we want the best resolution. In the abdominal situation we use lower frequency stages, 2,000,000 cycles per second, where we can afford to lose some resolution but it's important to see into the liver, for example, to a great depth.

<**McCready over diagrams and readings showing how ultrasound waves function**>

Each time the ultrasound perceives a change in tissue density, a certain amount of the sound energy is reflected back towards the transducer. Sound waves behave rather like light waves, giving the best reflection when the waves hit the structure or change in density perpendicularly. The best reflections are found with the maximum change in density, for example, when moving from the uterus into the fluid surrounding a foetus, then into the foetus. This type of situation shows the best pictures.

In the A-scan technique, the size of the sound reflection is demonstrated by the peak on the oscilloscope tube. The initial bang on the left is caused by the transducer switching into the receive mode while it is still ringing after transmitting the pulse. Since we know the speed of the spot moving across the oscilloscope tube and we know the velocity of the sound actually inside the patient, we can relate the two and measure the distance within the patient by measuring the distance between peaks on the oscilloscope tube.

One of the first applications of A-scan ultrasound was in finding the midline within the skull cavity. In this diagram you can see the large peak in the centre which is due to the midline structure within the brain. If a tumour grows within the skull cavity, this will displace the midline to one or other side, and it's a very simple technique to show this movement by the alteration of the peak produced by the midline structures. This kind of technique can be very important in an accident department […]

<**McCready over film showing doctor using ultrasound on a man's head**>

[…] for example, where one may have bleeding on one side of the skull, and this of course will push the midline structures across to the other. Another possibility is in finding an unsuspected tumour, a tumour growing in one side of the skull again will push the midline structures across, and there's a very simple technique which will show this movement.

<**McCready over image of ultrasound scan and then to camera**>

Another very nice application of this type of technique is in the measurement of the size of the foetal skull. Using this technique, one can assess the age of the foetus and estimate its time of delivery. Of course, this is very important nowadays when many women are being induced before they might otherwise have produced the baby.

<**McCready over diagram of B-mode presentation of ultrasound waves, then film of this process in practise**>

In what we call B-mode presentation, the reflections this time are demonstrated as bright areas instead of peaks. To make a picture of the internal structures, the transducer is linked to a mechanical arrangement. As one moves the transducer backwards and forwards, we can make a trace on the oscilloscope follow the sound of the transducer and the line of the sound waves. By tracing a whole series of lines over the oscilloscope tube, each with its bright spots indicating a change in structure, one can gradually pick up a picture of internal structure of the patient.

<**McCready over diagram showing grey scale readings, then a comparison between an older reading and a grey scale reading of a liver**>

The big advance in ultrasound over the past year or so has been the development of so-called grey scale ultrasonography. Until recently the electronics and the oscilloscopes were such that only very large echoes were displayed; this, in fact, is rather good for obstetric work where one is concentrating on either tissue or fluid inside the uterus. However, for tumour work one is more anxious to display as much detail as possible. In grey scale ultrasonography, all the small echoes are displayed with some preference being given to the smaller reflections.

In this picture, you can see a normal liver, shown first of all with the older type of display and then with the new grey scale technique, I think you will agree that the improvement is obvious.

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<**McCready over film of an ultrasound scan taking place**>

The actual process of taking the scans is quite easy although considerable experience greatly improves the quality of the pictures. Some oil is sprayed over the abdomen enabling the sound waves to pass straight from the transducer to the patient. A series of sweeps across the patient is used to build up a picture on the oscilloscope monitor. A permanent photograph can be taken from a second tube. When the doctor is carrying out the examination he refers constantly to the A-scan presentation, this gives him some idea of the absorption characteristics of the tissue he is studying and it can tell him whether he is finding fluid or pus or perhaps even gallstones.

With the ultrasound technique we can study most of the abdominal organs – tumours and cysts and lumps in the liver, the spleen, the kidney, pancreas, bladder and lymph nodes. We can also study lumps and bumps in and around the thyroid gland. In most cases we would take an isotope scan first of all to find the lump and then we would use the ultrasound technique to get more anatomical detail and then to try to make a differential diagnosis.

<**McCready to camera, then diagrams and scans showing ultrasound of the liver**>

I would like now to show you how the ultrasound techniques are applied to each organ in turn and let you see how ultrasound, in fact, helps to make the clinical diagnosis. One of the most important organs in tumour localisation work is the liver because this is the organ where many secondaries from a variety of cancers can be located.

The ultrasound technique of scanning the liver is very simple. A series of longitudinal sweeps are made, starting under the intercostal margin and working from the lateral side towards the medial side. You will remember earlier on in the lecture seeing such a liver scan being carried out. This is a picture showing the normal texture of the liver – you have the skin at the upper right side of the picture, the diaphragm is the curved white line to the left and the kidney is at the bottom of the picture on the right. You can see one or two blood vessels in the liver, giving you some idea of the high degree of resolution we can now achieve.

Sometimes it's difficult to distinguish vessels from tumours or cysts and normally we take a series of pictures, trying to follow the vessels from the outside of the liver towards the centre of the liver. In this set of pictures the centre of the liver is the top picture, and the lateral part is in the bottom right picture where you can also see part of the kidney. You can see how the vessels congregate towards the centre of the liver in the top picture.

Space-occupying lesions in the liver fall into two main categories: those that are benign and those that are malignant. One of the benign causes of lesions in the liver is due to cysts and this particular picture shows a patient who had multiple cysts within the liver. Again you have the skin at the top and the diaphragm at the back and the patient's liver is in the bottom of the picture. We know that these are cysts partly because they're nice and circular in their appearance and also partly because there's less absorption of the ultrasound in the fluid inside the cyst, and this causes the areas with increased echoes behind the cysts, and you can see this on the bottom of the picture towards the left.

This patient presented with a temperature and we suspected that she may have an abscess. Again, on the ultrasound picture on the right you have the skin at the top right, the diaphragm on the right and the patient's back toward the bottom of the picture. The isotope scan we took first of all showed a cold area on the top left and we did the ultrasound scan following this to try and make the ultrasound diagnosis. The ultrasound scan shows a black area just below the diaphragm with a little structure inside. And the combination of the clinical situation plus this picture added up to an abscess which, in fact, turned out to be the case.

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This patient had a primary cancer of the breast and we were looking for liver secondaries. Again we have the skin at the top, the diaphragm at the left and a little bit of the kidney showing in the bottom right part of the picture. Posteriorly at the patient's back under the diaphragm, you can see a large area with reduced echoes and the outline of this and its appearance led us to believe that this was a secondary from the cancer of the breast, and again this turned out to be the case. Look at the small vessels just proximal to this lesion and you again can see the high resolution achievable with the ultrasound technique.

<**McCready over various ultrasound scans of major organs**>

This isotope scan shows a cold lesion in the picture at the bottom. On the top left picture you can also see a cold area on the inferior edge of the liver. Now, we thought this might be due to the gallbladder rather than a cancer and the next picture shows that this, in fact, was the case. The ultrasound scan shows a large fluid containing area lying just beneath the skin. At the back of the picture you can see the kidney again and you can see a small duct leading from the gallbladder. So it was very easy in this case to be sure that that cold lesion on the isotope scan in fact wasn't cancer but was due to the gallbladder being slightly dilated.

One of the causes of dilatation of the gallbladder is due to stones in the duct that leads from the gallbladder into the gut. In this picture you've got a gallbladder which is not too large, but lying at the bottom of the gallbladder you can see a white reflecting area which this time is due to a gallstone. Behind that you can see a dark area which is the result of the acoustic shadowing, the gallstone actually absorbing the ultrasound and causing no echoes behind it.

We can also study the kidneys. The right kidney is easiest to see as it lies behind the liver. On the left-hand side you've got a normal picture, again the skin at the top, diaphragm at the left. Inside the kidney you can see the calyceal pattern and the cortex around it. On the right side, the same type of approach shows a very large cyst lying in the upper pool of kidney. Again, we know that this is a cyst because it's circular and contains no echoes or structure within it. A tumour of the kidney looks quite different; again a picture of the right kidney taken through the liver, skin at the top, patient's back at the bottom of the picture. This time, the whole of the kidney area is replaced by highly reflecting structure and this, in fact, was due to a primary cancer of the kidney.

Tumours in or around the bottom of the abdomen are more difficult to diagnose because of the presence of bowel gas. In spite of this, one can see various lesions involving the bladder and the female reproductive tract quite clearly. In this picture you have the skin at the top, it's a longitudinal section, the bladder lies to the right and contains urine and there is no structure within it. Behind the bladder, towards the bottom of the picture, you have a large circular mass, and this, in fact, turned out to be due to a fibroid. From the ultrasound appearances alone it would be difficult to differentiate this lesion from a cancer, but obviously one takes into consideration the clinical appearances and makes the diagnosis from several factors.

Well, ultrasound can be used for various other organs including the breast and the thyroid and lymph nodes in and around the aorta and so on, but I think it would be more interesting now to ask my colleague, David Cosgrove, to take me through an actual case history to show you how ultrasound helped make the diagnosis in conjunction with the other techniques.

00:19:43:11

<**Dr David Cosgrove to camera**>

I'd like to present the case of a 53-year-old housewife who presented with jaundice to try and show you, using her as an example, how ultrasound was able to make a contribution to solving her problem.

She started with, six months before we saw her, with losing weight. And despite a good appetite, by the time we saw her she had in fact lost two or three stones. A month before we saw here she developed diarrhoea, and then two weeks before she'd begun to turn yellow. The jaundice had become progressively more severe although she was, in fact, quite comfortable with her pain and felt quite well in herself. Clinical examination revealed a mass in the right upper quadrant of her abdomen but apart from the jaundice nothing else of significance was found, and so she went on to a series of tests, both blood tests and urine tests, to try and elucidate further the cause of her jaundice. These tests confirmed that she was jaundiced and they revealed, not unexpectedly, that she had a pattern of obstructive jaundice, meaning that the bile was being formed quite normally but was not escaping from the liver to be passed down into the gut.

The problem with this group of tests is that although they may well be able to tell you the jaundice is obstructive, they're not very good at distinguishing the level of the obstruction and this has important management and clinical significance. The problem is that you may get jaundice due to a lesion in the main drainage system from the liver causing jaundice, or you may get a biochemical disturbance actually within the liver itself.

<**Cosgrove over diagram of liver, then back to camera**>

The diagram shows the point I'm trying to make. The liver is in this region here and these are the main bile ducts joining together from the left and right lobes to form the common duct passing down through the head of the pancreas and draining into the duodenum which is shown here. The gallbladder's here, acting as a reservoir. A lesion anywhere in this part of the system will cause jaundice but likewise a lesion at cellular level, within the liver up there, may produce precisely the same pattern and it may be quite impossible to distinguish these biochemically.

Therapeutically, of course, the problems are entirely separate. The biochemical type of jaundice occurring due to a lesion within the liver cells cannot be cured surgically and needs medical treatment. So this lady went on to a series of other tests to try and elucidate these. One of the most dramatic and useful in trying to sort out the anatomy of the biliary tree is to introduce a contrast medium into the bile ducts. If the obstruction is minimal then it's possible to get contrast in by relying on the liver's own metabolism, and you can do this by asking the patient to take orally a contrast agent which is then excreted by the liver, or you can inject them into the blood stream and rely on the same mechanism.

Unfortunately, when jaundice is very severe and the obstruction is complete or nearly so, this technique fails and then one has to resort actually to injecting a dye directly into the liver ducts. This involves passing a needle through the skin, through the liver capsule and into the dilator ducts within the liver. It produces beautiful pictures like the one shown here […]

<**Cosgrove over x-ray picture**>

[…] which is a picture of an x-ray – the patient lying on her side and the spine at the lower part of the picture. And you can see on the left the syringe and the needle, passing right through the skin and through into one of the main ducts within the liver. The complex of ducts is very clearly outlined and these are dilated and abnormal, and then passing down to the left is the common duct, towards the duodenum which would be about there. Well, this technique certainly produces excellent images […]

<**Cosgrove to camera**>

[…] and it outlines the relevant anatomy very clearly. But it does involve puncturing the liver, and if the biliary fluid is under pressure there's a danger that some of it may leak back and contaminate the peritoneal space. This produces bowel peritonitis which is a rather dangerous condition and, in fact, it is normal practise, when undertaking this so-called trans-hepatic cholangiogram, to have theatre facilities ready so that if dilated bile ducts like this are demonstrated, the patient can be taken straight through and an immediate exploration performed. Well, that's obviously not easily arranged and to be avoided if possible. And another x-ray technique has been developed which involves cannulating the common bile duct by passing one of the newer fibre optic endoscopes, which the patient swallows, it's then passed through the stomach and into the duodenum.

<**Cosgrove over diagram of liver**>

And again, going back to the diagram, the fibre optics endoscope comes right through the stomach into the duodenum, here, and then a small cannula is passed through the orifice of the common duct in this region, here, and a contrast medium is injected back to outline the ducts. This technique is very useful […]

<**Cosgrove to camera**>

[…] – it's very difficult for some patients to tolerate the endoscope and sometimes it's difficult to cannulate the duct itself, and although it's pretty free of risk, it may be difficult actually to perform. It's also quite a skilful investigation and not all that many radiologists are able to undertake it.

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<**Cosgrove over ultrasound scans leading to diagnosis of a pancreatic tumour**>

Now, ultrasound will often enable the same sort of information to be obtained but very much more easily. This section was obtained from this patient and it shows a view of the gallbladder, which is the dark pear-shaped region to the right of the picture there; it has behind it a brighter region which indicates to us it's a fluid-containing mass. To the left, in the main substance of the liver, is a complex of dilated ducts, the black lake-like regions and on the extreme left of the view we've shown the left atrium. The next section is a little bit further over to the right, same patient, and it shows a stellate complex of ducts in the right lobe of the liver and these are the dilated right lobe radicals of the system; posteriorly is the right kidney.

So these longitudinal views showed us that this patient had obstructive jaundice, we could deduce that the obstruction was occurring at a site outside the liver but were not able, at this stage, to delineate the source of the obstruction. However, the transverse views gave us the additional information that we needed. In this view you can see posteriorly the black region which is the spine and anterior to it is a rounded black area which represents a mass in the region of the head of the pancreas. Following these investigations, this patient came to laparotomy and was found, indeed, to have a mass in the pancreas, in this region here, which was obstructing the common duct and causing dilatation of the whole system back into the liver. And biopsy of this mass revealed malignant cells, telling us that this was a tumour of the pancreas.

The operation was designed to relieve the obstruction by anastomosing the gallbladder to one of the lobes of the small intestine so that the bile had another means of egress and alternative means of treatment is being directed at the tumour itself. The patient's now quite a lot better, the jaundice is disappearing fast and she's having alternative treatment.

<**Cosgrove to camera**>

Well, I think this case illustrates how it's possible, using ultrasound, to obtain the essential anatomical information in a patient with obstructive jaundice. It can be done very easily, it's pain-free and simple for the patient. It's certainly true that the other investigative techniques that I outlined could produce the same sort of information but not without risk and all of them with some discomfort. I think it's amazing that in the current, fairly crude state of development, ultrasound is able to provide this kind of diagnostic information. It's a subject that's advancing fast and in our team we have got several approaches to try and advance the diagnostic applications of ultrasound and to improve our scientific understanding of the basis of what's going on.

To explain and outline some of these, I'd like to hand over now of one of my colleagues, David Nicholas.

00:28:44:00

<**David Nicholas to camera**>

At present, we have a very limited understanding of the tissue structures which attenuate and reflect the ultrasonic sound waves, and today I would like to concentrate on this aspect.

We are trying to investigate this by a method which is analogous to x-ray diffraction.

<**Nicholas over animated diagram showing diffraction pattern of ultrasound waves**>

In principle our method involves the collection of ultrasonic echoes from a volume of tissue that we are interested in. We then study the way in which the received echo strength varies as we rotate the tissue volume, thereby altering the orientation of the volume with respect to the viewing direction. The result is a diffraction pattern similar to those obtained in the analysis of crystals by x-rays.

<**Nicholas over film of laboratory work analysing ultrasound echoes from liver tissue**>

In our laboratory set-up, this method has been applied to a variety of types of human tissue. A small computer controls the experimental procedure and data acquisition. In a water-filled sound tank we can see a specimen of normal human liver tissue being investigated. An oscilloscope indicates the variation of the echo strength as the specimen rotates. In order to obtain a visual record of the ensuing pattern, a light-sensitive chart recorder monitors the varying echo strength as a function of rotation. The variations seen on these traces are due to the individual scatterers within the tissue volume, each contributing a reflected wave, the sum of these waves resulting in alternate constructive and destructive interference, the former being depicted as the peaks on the right of the trace. We have reason to believe that the so-called lobular structure of the liver is responsible for this typical liver diffraction pattern.

<**Nicholas over graphs showing diffraction patterns of different tissues**>

An exciting feature of this method of analysis is the significantly differing patterns produced when different tissue types are investigated. Here, for example, are the typical patterns obtained when these specific tissues are investigated. For cancer diagnosis, this approach to the characterising of tissue structure could be of immense value since malignant tissues are well known to exhibit a differing structure from that of their normal tissue of origin.

Here, for example, is the diffraction pattern obtained from a volume of liver tissue containing small secondary tumours, and, for comparison, the pattern associated with that of the normal liver in which they were growing. This kind of approach to categorising tissue structure is more than just a useful laboratory exercise. In principle, it can be applied safely and painlessly on live subjects, and we are at present experimenting with one of a number of approaches.

<**Nicholas over film demonstrating a hybrid ultrasonic scanner**>

The machine in operation is a hybrid ultrasonic scanner equipped with a scanning arm which permits the investigation of specific tissue volumes from varying directions. This is achieved by constraining the transducer movement using a pantograph arrangement. A normal sectascan is first produced of a general area of interest. Then, the clinician selects an area of tissue for diffraction analysis. This is achieved by mechanically altering the pantograph, thus constraining the investigation to the specific tissue depths at which that tissue volume is situated. Re-scanning now produces a sectascan pivoting about the region of interest and a complimentary diffraction pattern. In this subject the diffraction pattern is typical of normal liver tissue.

This is just one example of the information available if we can get to grips with the basic science of the subject. One can, justifiably, expect to see the future of ultrasound presenting not only better anatomical pictures but also new information about the structure and pathology of living human tissues.

<**McCready to camera**>

Well, you've seen how powerful a clinical tool ultrasound techniques are. They have the special attraction that they don't involve injections, a very nice thing from the patient's point of view. You've also seen that we're just at the beginning of understanding the scientific basis behind ultrasound, and that with a bit more research we should be able to make more accurate diagnoses and a more objective point of view.

Who knows – one day we might even make ourselves redundant.

<**End credits**>