Fig. 3: A CT image showing calcified subependymal nodules (the bright white areas adjacent to the black areas of fluid). The area shown by the arrows is a cortical tuber that is distorting the normal brain tissue.

Fig. 4a: MR images before the injection of contrast agent. The grey area indicated by the arrow is a subependymal giant cell astrocytoma.

Fig. 4b: The patient has been given contrast and the subependymal giant cell astrocytoma has enhanced so it is now clearly seen as a large white area.(arrowed)

Fig. 5: A MR image with several cortical tubers at the edges of the brain seen as ill-defined white areas.

Dr Elspeth Whitby and Professor Paul Griffiths
Section of Academic Radiology, University of Sheffield 1999
Revised 2010 by Professor Paul Griffiths

Further information on TSC and the work of the Tuberous Sclerosis Association can be obtained from our website at: www.tuberous-sclerosis.org

While every effort is made to ensure that our publications are correct, please note that some information may change after the date of printing. Information in this leaflet is not intended to be a substitute for medical advice from your own doctors, who know your individual circumstances. We strongly recommend you talk to your doctor, and share the above information. The TSA cannot be held responsible for any actions taken as a result of using TSA information resources.
Tuberous sclerosis complex (TSC) affects between 1 in 7,000 to 10,000 live births.

It affects many of the body systems. Outwardly you may not know that someone had TSC and the diagnosis is usually made on what the person tells the doctor about the problems they have and the findings on examination by the doctor. However many patients will be referred for imaging of their brains to confirm the clinical diagnosis, evaluate the extent of the abnormality, look for associated abnormalities and to follow up patients with known abnormality.

The common initial problems in TSC are seen in the brain and this can also be the site of important complications. This leaflet gives information on the range of imaging techniques available and what is involved in having those tests.

Imaging department (previously called x-ray department) has various methods of imaging.

Plain film
This involves the patient standing next to a stand holding a flat cassette that contains an x-ray film, or lying on a table that has a special tray below to hold the cassette and film whilst the radiographer positions the x-ray tube over the area of the body to be imaged. The patient will be asked to stay very still for a few seconds whilst the x-ray is taken. The patient will hear some noise from the machine but will not feel anything. The plain x-ray has limited use in patients with TSC. It sometimes shows up the areas of calcification in the brain. It has been replaced by CT scanning and is not routinely used in people with TSC.

The CT scanner
This is useful in imaging the brain. CT stands for computerised tomography. Like the plain film the CT scanner uses x-rays that are produced from a series of tubes set around the edge of an open ended tube. The patient lies with their head in the tube and each x-ray passes through the patient (Fig. 1). The patient will move through the tube during the scan so that the x-rays pass through small areas of the brain each time.

The table will move the patient who just needs to lie still. The patient does not see or feel anything during the process but will be aware of the noise the machine makes. Each x-ray is then detected after it has passed through the patient and by means of computer analysis of the amount of x-rays absorbed when it is detected we can build up a picture of what the x-ray has passed through. We will then have lots of tiny blocks of information all indicating a small bit of the brain and the combination of these gives us the image seen.

It is sometimes necessary to give patients an injection of a contrast agent into a vein in their arm to help see different brain structures clearly, particularly blood vessels. The contrast agent used contains iodine and should not be given if the patient is allergic to iodine. If the patient is a diabetic and on tablet medication they should tell the people doing the scan as the contrast may react with one type of tablet used to treat diabetes. Care should also be taken if they suffer from asthma or have a history of severe allergies. Some people have a reaction to the contrast but this is uncommon and usually mild. Possible side effects include a transient warm feeling, a funny taste in the mouth and nausea (feeling sick) these only last

Fig 1 A CT Scanner
Brain Imaging in TSC

a few minutes. Occasionally a patient may develop a rash, or have slight difficulty in breathing. It is very rare to have a severe side effect but emergency treatment is always available in the scanning rooms in case this happens.

The MR scanner.
The magnetic resonance scanner uses a magnet to provide images. To obtain the information we need to build up the images of the brain we need to apply the magnetic field lots of times, sometimes several hundreds of times. Each time we obtain a small amount of information. The scan can take up 30 minutes to obtain the information we need. MR scanners are very large and noisy machines. They look like large polo mints and the patient lies in the central hole (Fig. 2). Many centres have a facility allowing the patient to listen to music during the scan and they may be allowed to take their own music with them. In some centres a member of their family or a friend may be allowed into the room during the scan to keep them company.

As the scanner is a very large magnet, much larger than any magnet they will have handled, the patient will be asked to remove any magnetic objects from their pockets and clothes. These include keys and credit cards (as the magnet will delete the information held on the magnetic strip on the reverse of the card). In addition any metal on or inside their body may not only be dangerous but also degrade the image so it is important that the people doing the scan are told if the patient has had any operations or artificial body parts, such as replacement joints or a heart pacemaker.

MR gives very good images of the brain but sometimes it is necessary to improve these images further to help work out if there are abnormal areas present and if so what they are. To do this the patient may be given a contrast agent called Gadolinium. This involves injecting a small amount of contrast agent into a vein in the arm or hand. The blood carries the contrast to the brain and it will be seen in areas of high blood flow and some abnormal areas. Gadolinium is a very safe contrast agent and in the doses used the side effects are minimal. The possible side effects include mild headaches, feeling sick, vomiting and on rare occasions a rash. Gadolinium should not be used in any patient who suffers from any blood disorder e.g. thalassemia and sickle cell disease, or if they are pregnant. Sometimes it is necessary to have sedation or a general anaesthetic for the duration of the scan. This is because the scans can take a long time and some people are unable to keep still for the length of time required. In addition some people find the machine claustrophobic and sedation helps overcome this problem.

Brain abnormalities seen in TSC
The brain changes in TSC are variable. Below are several examples of the different things we see in the brain in TS.

Subependymal nodules – these usually contain calcium and are clearly seen on CT scan images as white areas. These are small, about 1 cm in diameter. If they do not contain calcium they may not be seen on CT images but will be seen on MR images. These areas may grow and if they become large they may block the normal flow of fluid around the brain causing a
build up of pressure and dilatation of the fluid filled spaces in the brain (hydrocephalus). If this occurs they need to be removed by a specialist surgeon. We can only tell if they have grown by doing several scans over a period of time hence the importance of regular check-ups.

**Subependymal giant cell astrocytomas** – these develop from the subependymal nodules, they are usually larger but the best way of telling that a subependymal nodule has become an astrocytoma is that it has enlarged since the previous imaging and in some cases has started to obstruct the flow of CSF (the fluid that surrounds the brain) resulting in hydrocephalus (dilated areas of brain that contain fluid). They appear on the images like the subependymal nodules only bigger (usually over 12mm).

**Cortical tubers** – These are found in the upper part of the brain and appear as an abnormal mass of tissue within the brain. They can also calcify. These are best seen by MR scans. These may be large and distort the normal brain tissue. It is likely that tubers are the cause of fits in TSC.

**Abnormalities of the blood vessels in the brain** – a few cases have been seen where there are abnormal blood vessels and occasionally this has caused the individual to suffer a stroke.

### Imaging appearances

**Subependymal nodules** are often calcified and are seen as white areas on the CT scan images. (see Fig.3) If they are not calcified they are harder to see but are seen as area where the normal shape of the brain is distorted. They are easily seen on MR scans where they are a different shade of grey to the surrounding brain tissue and on some sequences used in the imaging process they show up white. Administration of gadolinium (a contrast agent given via a vein in the arm) causes these areas to become white on the scans and therefore easily visible.

**Subependymal giant cell astrocytomas** – these appear the same as subependymal nodules only larger. (see above). They enhance (become brighter) when the patient is given gadolinium. (Figs. 4a & 4b).

**Cortical tubers** – these may calcify and show as white areas on a CT scan. They tend to occur in the upper part of the brain. On MR images they are bright and can cause distortion of the surrounding brain tissue. (Fig.5).

### When is each method of imaging used and why?

**a) Radiation Dose**
A Chest x-ray is used as a reference point and gives the patient a dose of radiation each time a chest x-ray is taken, this dose is 1 unit. A CT scan of the brain gives the patient a radiation dose 100 times that of a chest x-ray i.e. 100 units. It is important to keep the radiation dose to the patient as low as possible but to obtain all the information necessary to diagnose and treat the patient. MR does not use any radiation.

**b) Imaging**
Initially a patient may have a CT scan and a MR scan. The CT scan will show areas of calcification not seen on a MR scan and is an important method of imaging the patient at the time of diagnosis. The MR scan will provide detail on the other brain changes seen in TSC. For follow up of the brain changes MR is the method of choice as this does not involve radiation.