3.1 CLASSIFICATION OF PRIMARY BRAIN TUMOURS

3.1.1 Introduction

Tumours can be classified (Osborn 1994) by different taxonomic methods. These include classification by histology. In classification by histology, tumours are divided into two main classes - primary brain tumours and metastatic brain tumours. The term primary brain tumour encompasses neoplasms and related mass lesions that arise from the brain and its linings. Primary brain tumours are again classified into various classes depending on the tissue of origin. There are other taxonomic methods of classification of brain tumours including classification by age of the patient and classification by anatomic location. Since the gold standard in diagnosis is histology, this classification taxonomy has been adopted for these studies.

The incidence of brain tumours in the general population of the U.S.A. has been roughly estimated at 4.5 per 10,00,000 persons (Osborn 1994). The largest single group of brain tumours is astrocytomas, followed by meningiomas, pituitary adenomas and schwannomas. The most important factor in establishing appropriate differential diagnosis for an intra-cranial mass is location followed by age of the patient. Precise anatomical localisation of an intra-cranial neoplasm is of fundamental
importance in that through knowledge of such information one can often be specific about the diagnosis and prognosis of the lesion (Juhl and Crummy 1987).

3.1.2 Classification By Histology

Despite many efforts, there is no universally accepted pathologic classification of brain tumours. A modification (Osborn 1994) of the 1993 revision of the World Health Organisation (WHO) classification and Russel and Rubinstein classifications has been used in this thesis.

Brain tumours can be classified as primary or metastatic tumours, depending on whether the tumour cells belong to the brain parenchyma or to some other part of the body. Primary brain tumours include neoplasms and related mass lesions that arise from the brain and its linings. Non-neoplastic intracranial cysts and tumour-like lesions are also included, along with pituitary tumours and local extensions from regional tumours (e.g., craniopharyngioma and chordoma) that arise from adjacent structures such as the skull base.

Nearly two thirds of all tumours occurring in the brain are primary brain tumours. They can be further divided into two classes as glial and non-glial tumours, depending on whether they are of neuroglial or non-glial origin.

Neuroglial tumours are the largest group of primary Central Nervous System (CNS) neoplasms. Glial tumours are of four main classes: astrocytomas, oligodendrogliomas, ependymal tumours and choroid plexus tumours. Astrocytomas include fibrillary astrocytoma, benign astrocytomas, anaplastic astrocytoma, pilocytic astrocytoma, pleomorphic xanthoastrocytoma and subependymal giant cell astrocytoma. Ependymal tumours include papillary and cellular ependymomas, anaplastic
(malignant) ependymoma, myxopapillary ependymoma and subependymoma. Choroid plexus tumours include choroid plexus papilloma, choroid plexus carcinoma and choroid plexus xanthogranuloma.

Non-glial tumours are of nine main classes: neuronal and mixed neuronal-glial tumours, meningeal and mesenchymal tumours, pineal region tumours, embryonal tumours, cranial spinal nerve tumours, hemopoetic neoplasms, pituitary tumours, cysts and tumour like lesions, and local extensions from regional tumours. Tumours of the anterior pituitary gland are technically not brain tumours.

Metastatic tumours arise from sources outside the CNS and account for approximately one third of all brain tumours. The histologic spectrum and general locations of primary brain tumours are quite different in children compared to adults.

3.2 QUALITATIVE IMAGING FEATURES OF SOME BRAIN TUMOURS

The qualitative imaging features of some commonly occurring primary brain tumours are given below.

3.2.1 Meningiomas

Meningiomas are extra-cranial tumours that arise from the arachnoid. The majority of them are benign. The common locations of meningiomas include sites along the superior sagittal sinus particularly in the posterior frontal and parietal areas and adjacent to the convexities of the cerebral hemispheres a short distance away from the midline. Grossly, meningiomas vary in shape from a globular configuration to a flat type of growth (Juhl and Crummy 1987).
Most meningiomas are iso- or slightly hypo-intense related to cortex on T₁ weighted studies, although signal on T₂ weighted images is variable. Nearly all meningiomas enhance rapidly and intensely following gadolinium administration. The variable imaging features of meningiomas may not accurately reflect histologic subtypes. Although the imaging features of most meningiomas are characteristic, some meningiomas mimic benign tumours such as schwannoma, and others resemble malignant neoplasms such as anaplastic astrocytoma (Osborn 1994).

An example of the MR images of a cerebropontine angle meningioma is shown in figure 3.1. It is iso- to hyper-intense on the T₂ weighted GRASE image. It is also iso- to hyper-intense on the T₂ weighted FLAIR image. It is hypo-intense with respect to normal tissues on the T₁ weighted SE image and enhances well after the administration of gadolinium contrast agent (described in section 4.2.1).

Another example of a meningioma is shown in figure 3.2. It is iso-intense on the T₁ weighted image and shows intense enhancement on the post-gadolinium image. There is a large area of surrounding oedema.

3.2.2 Astrocytomas

Astrocytomas may be very slow growing, diffusely infiltrating lesions, which are often associated with a survival of five to ten years or longer, to the more common malignant lesions that produce death within a few months after symptoms become apparent (Juhl and Crummy 1987). Astrocytomas are a histologically heterogeneous group of primary brain tumours that are both graded and classified. The following are the qualitative features of different grades of astrocytoma on MR images (Osborn 1994).
Figure 3.1 A meningioma in the cerebropontine angle.
(a) $T_1$ weighted GRASE scan (b) Post-gadolinium $T_2$ weighted SE scan (c) $T_1$ weighted FFE scan (d) post-gadolinium $T_2$ weighted FFE scan. (Clockwise from top left).

Figure 3.2 MR Images of a meningioma.
Low grade Astrocytomas (Kernohan grade I and II) are iso- to hypo-intense compared to adjacent brain on T₁-weighted images and appear homogeneously hyper-intense on T₂-weighted images. Most low grade astrocytomas eventually undergo malignant degeneration. In these cases contrast enhancing foci within an otherwise benign-appearing mass may be the initial harbinger of more aggressive disease.

Anaplastic Astrocytoma (Kernohan grade III) account for one third of all astrocytomas. They are poorly delineated lesions that have heterogeneous signal intensities on both T₁ and T₂-weighted images. Mixed iso- to hypo-dense areas are seen on the T₁-weighted sequences. Some haemorrhagic foci may be present. A common appearance on T₂-weighted images is a central core of hyper-intensity surrounded by an iso-intense rim with peripheral finger-like high intensity projections secondary to vasogenic oedema. Anaplastic Astrocytomas have moderate mass effect. Marked but irregular peripheral ring-like enhancement following contrast administration is usually evident. Uncommon imaging appearances of Anaplastic astrocytomas include a focal, cyst-like, non-enhancing mass or cortical mass that resembles infarct or encephalitis.

Glioblastoma Multiforme (GBM) (Kernohan grade IV) is the most common CNS neoplasm. MR reflects the pathological heterogeneous nature of GBMs. T₁-weighted images show a poorly delineated mixed-signal mass with necrosis or cyst formation or a thick irregular wall. Marked but inhomogeneous contrast enhancement is present in the major of GBMs. T₂-imaging studies show a very heterogeneous mass with mixed cellular components, central necrosis and haemorrhage of different ages. Peripheral oedema is typically striking. Tumour margins often blend imperceptibly with the surrounding oedema and actually represent “tumour plus oedema”. Neoplastic cells can be found far beyond demonstrable T₁ signal abnormalities.
The astrocytoma in figure 3.3 is iso-intense to grey matter on $T_1$ weighted image, hyper-intense to grey matter on $T_2$ weighted image. It does not show any enhancement after gadolinium administration.

3.2.3 Pituitary Adenomas

Tumours of the anterior pituitary gland are technically not brain tumours but are included in this study as they arise within the cranium. Pituitary microadenomas are hypo-intense compared to normal pituitary on dynamic contrast-enhanced MR scans. For pituitary macroadenomas on the other hand a signal like that of the cortex on $T_1$- and $T_2$-weighted images, is the most common pattern. Variable signal intensity is observed if haemorrhage, necrosis or cyst formation is present.

Figure 3.4 shows a pituitary adenoma. It is iso-intense on the $T_1$ weighted image and hyper-intense on the $T_2$ weighted image. It shows good enhancement after gadolinium administration.

Sometimes meningiomas occur in the pituitary region. The treatment approach for primary brain tumours depends on the type of tumour, location and size, among other factors. Hence discrimination, prior to surgery, between pituitary adenomas and meningiomas in the pituitary region, would be of value to both the patient and the neurosurgeon.

3.2.4 Craniopharyngiomas

Of all sellar masses, craniopharyngiomas have the most heterogeneous MR imaging spectrum. The signal is highly variable. Craniopharyngiomas enhance strongly but heterogeneously following gadolinium administration.
Figure 3.3 MR Images of an astrocytoma.
Figure 3.4 MR Images of a pituitary adenoma.

(a) $T_1$ weighted GRASE scan (b) $T_2$ weighted FLAIR scan (c) $T_1$ weighted FFE scan (d) post-gadolinium $T_1$ weighted FFE scan. (Clockwise from top left).
3.3 QUANTITATIVE ANALYSIS OF BRAIN MR IMAGES

It is now well known that a variety of neoplasms display different spin-lattice relaxation time ($T_1$) and spin-spin relaxation time ($T_2$) values (Farrar and Becker 1971) from the corresponding normal tissue (Kjaer and Henriksen 1988, Taylor et al., 1988, Araki et al., 1984). These different relaxation times occur with tumours of diverse histological type. The possibility of pulsed NMR being adapted to quantification and characterisation in terms of relaxation rates was investigated by several researchers (Rinck et al., 1985). Accurate measurement of $T_1$ is influenced by the TR value of the pulse sequence applied (Kjaer and Henriksen 1988). The reported in-vivo measurements of $T_1$ and $T_2$ showed considerable variations (Just et al., 1988). Several factors have been shown to contribute to an explanation of this observation, some of which are related to the dynamics of the tissue being investigated, while others may be induced by the measurement strategy (Breger et al., 1989, Rinck et al., 1985). Studies show that most demographic, lifestyle and medical history factors have little effect on the $T_1$ and $T_2$ relaxation parameters of the cerebral white matter, caudate nuclei, putamen or thalamus. Although age has a statistically significant effect on $T_1$ and $T_2$, the magnitude of the effect is not large. The $T_1$ regression coefficient for white matter was approximately 0.67 ms/year which corresponds to about 35 ms (5%) lengthening in 50 years. The $T_2$ regression coefficient for white matter was about 0.1 ms (7%) lengthening in 50 years (Agartz et al., 1992, Agartz et al., 1991, Breger et al., 1991).

The work of Kjaer et al. (1991) and earlier work (Rinck et al., 1985, Mills et al., 1984) have shown that tissue characterisation by MR imaging based solely on relaxation time measurements alone seems to be of no value in the differentiation of intracranial tumours.
Cluster classification techniques have been used for volume measurement, yet little attention has been paid to how the choice of images for analysis affects the quality and ease of segmentation (Simmons et al., 1996). Simulation of MRI cluster plots has been used to choose suitable images for neurological segmentation of grey matter, white matter, CSF, and multiple sclerosis lesions using SE, IR and gradient-echo pulse sequences (Simmons et al., 1996).

Histogram-based cluster analysis methods have been used for automatic analysis of multi-parametric image data from several body slices simultaneously. Pattern recognition techniques were used on the data base to develop a software system for 3D segmentation visualisation, and classification of tissue structures (Handels 1995). Pattern recognition techniques have also been used for image segmentation (Bezdek et al., 1993).

Histogram analysis of exact T₁ and T₂ values measured for white and grey matter, CSF, muscle and fat was used to classify these tissue types in a database. Oedema and meningioma were classified with accuracy, while astrocytomas and glioblastomas were difficult to classify (Beenarding et al., 1995). Similar studies were used for the multi-spectral analysis of brain tissues (Fletcher et al., 1993, Vannier et al., 1987) and successfully classified grey matter, white matter, CSF, meninges, muscle and adipose tissues. Vannier et al. found that both supervised and unsupervised classification techniques yield theme maps which demonstrated tissue characteristic signatures. They also found that tissue classification errors found in computer-generated theme maps were due to subtle grey scale changes present in the original MR data sets arising from radiometric inhomogeneity and spatial nonuniformity (Vannier et al., 1987). Multi-spectral image analysis was originally developed for satellite imaging.
Texture analysis in quantitative MR Imaging has been used to obtain (Kjaer et al., 1995) a fine discrimination between white matter, cortical grey matter, and cerebrospinal fluid in the normal brain, and to separate the white matter from the tumour lesions. Separation of solid tumour tissue and peritumoural oedema was suggested for some tumour types. Mutual comparison of all tumour types revealed extensive differences, and even specific tumour differentiation turned out to be successful in some cases of clinical importance. The same authors reported that however, no discrimination between benign and malignant tumour growth was possible (Kjaer et al., 1995). Much texture information seems to be contained in MR images which may prove useful for classification and image segmentation. Tissue characterisation by MR Imaging, solely based on determination of $T_1$ and $T_2$ relaxation times, has proved rather disappointing with respect to specificity and clinical applicability (Schad et al., 1993, Kjaer et al., 1991, Just et al., 1988). These authors report that evidence indicates that tissue heterogeneity is a principal cause of the variation in the reported relaxation times, while imperfections in hardware and shortcomings in the experimental strategy seem to be of minor importance in this connection. Obviously, this strategy is not sufficient for in-vivo characterisation of complex biological tissues. In texture analysis, however, the estimations are based on pixel-wise calculations, giving a detailed and thus theoretically more substantial description of the tissues investigated, even when mean values of the texture information are used (Kjaer et al., 1995).

For volumetric measurements on MR images, statistical segmentation techniques such as texture analysis, maximum likelihood method, k-nearest neighbour rule, neural nets, fuzzy c-means clustering algorithms have been used with limited success (Friedlinger et al., 1995).