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PROJECT REPORT

Name : Dr. Somesh Desai

Programme : M.Ch. Neurosurgery

Month and Year of submission : November-2003

PROJECT REPORT

TITLE OF THE PROJECT:

ROLE OF STEREOTACTIC BIOPSY IN MANGEMENT OF INTRACRANIAL SPACE OCCUPYING LESIONS.

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Programme : ***M.Ch. Neurosurgery***

Month and Year of Submission : ***November- 2003.***

CERTIFICATE

I, Dr. Somesh Desai , hereby declare that I have actually performed/assisted all the procedures listed under report.

Place: Thiruvananthapuram **Signature**

Date: 7th November, 2003 **Name in capital letters**

Dr. SOMESH DESAI

Forwarded. He has carried out the project titled "Role of stereotactic biopsy in management of intracranial space occupying lesions".

Signature

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Contents

Introduction

Stereotactic techniques based on the experimental efforts of Horsley and Clarke have been applied in human Neurosurgery since the 50s Nevertheless the procurement of intracranial tumor specimens by stereotactic methods for the purpose of determining the histopathological diagnosis was not widely practiced until 1970's

At present time stereotactic biopsy is commonly used in the histological diagnosis of tumors located deep within the brain reducing the morbidity associated with nonstereotactic techniques. According to recent reviews this approach provides a diagnosis in 95% of cases although it must also be admitted that approximately 10% of the diagnoses are incorrect and do not agree with the results of the histopathological study of the tumor specimen obtained by craniotomy or at autopsy. Moreever it has been recognized that the tiny amounts of tissue obtained by sterotactic biopsy may be insufficient for correct diagnosis and may even lead to important error that can have an impact on the therapeutic management of the patient On the other hand over the last few decades new imaging techniques have been developed (CT Scan, MR, PET, SPECT) that are currently being applied to neurooncology and that, although not sufficient to successfully establish the exact nature of a brain tumor improve the diagnostic means without resorting to invasive methods. Thus we now consider it necessary to evaluate the advantages and drawbacks of stereotactic biopsy in the management of brain tumor patients. The objective of the present study is to reflect on our experience in a series of 140 patients who underwent stereotactic biopsy in the course of the diagnostic study of a presumed brain tumour

AIMS OF STUDY

1. Evaluate the yield of stereotactic biopsy in establishing pathological diagnosis
2. To study the pitfalls and associated complications of stereotactic biopsy

Review of literature

The current state of stereotactic surgery represents almost 90 year of developments in neurosciences and most recently, computer technology. Although the need for precise intracranial localization was recognized long ago, little progress in this endeavor was made until early in this century.

The technological basis of stereotactic surgery was introduced in a pioneering publication of Horsley and Clarke in 1903(Horsley and Clarke, 1908). They were the first to put the stereotactic principles into practice when they designed a frame for laboratory experiments. The conceptual break through was the development and integration of three-dimensional Cartesian coordinate system to the principal of stereotaxy. It is based on a concept that the location of any point in space can be defined by its relationship to three planes intersecting at right angles. Clarke described brain as a geometric body divided by three orthogonal planes: frontal, basal and sagittal using external skeletal points

Narabayashi have also been used extensively in different parts of the world.

COMMONLY USED STEREOTACTIC SYSTEMS: BASIC PRINCIPLES

Although a coordinate system for precisely describing targets within a geometric volume represents a cardinal feature of stereotaxis equally important is an accurate surgical apparatus for operating on those targets. Most stereotactic systems consist of coordinate frame and an aiming device. The frame is rigid and metallic and it is secured to the head using three or four screws that penetrate the outer table of the skull The aiming device represents an equally rigid collection of precision moving parts and a probe holder. The latter can be moved in either an angular or linear direction in order to direct a probe to any target previously defined within the coordinate system.

Most of the frame systems currently available use one of three geometric systems for stereotactic guidance: polar coordinate, arc radius, or focal point.

A) In **polar coordinate** systems, the target coordinates are Cartesian and expressed in millimeters from the reference point of the particular frame. Some of the first stereotactic frames including Clarke's 1920 modification of the 1908 system represented variations of the polar coordinate type. Other examples are Riechert Mundinger frame and BRW system

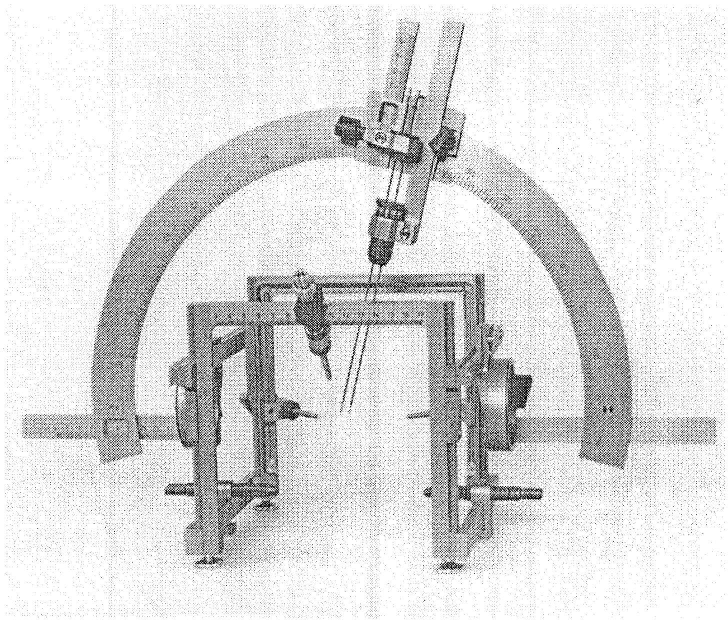
In Riechert Mundinger system radiographs are taken after placement of the head ring on the patient. These radiographs define the spatial relation of the lesion to the ring Separately the arc system is applied to a phantom ring in which a device indicates the relative location of the lesion as defined by the previous radiographs. The arc is adjusted until the tip of the probe touches the device. The arc system is then transferred to the patient with no further adjustment. This system remains popular in Europe today.

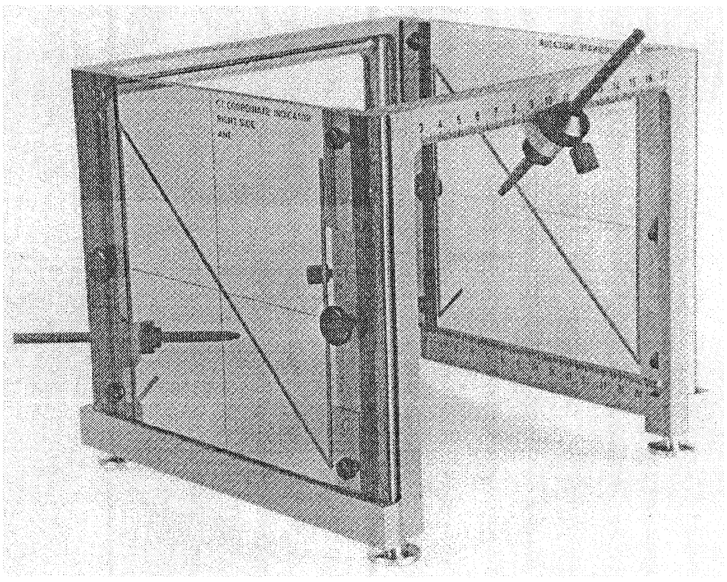
BRW arc guidance has a fixed vertical orientation to the aiming arc. This arc can then be rotated 360 degree in the horizontal plane (alpha) or pivoted 40 degree in the same plane (beta) The probe holder can be adjusted plus or minus 100 degree from the vertical (gamma) Lastly, the orientation of the probe holder to the arc can be pivoted plus or minus 55 degree in the plane of the arc (delta). The exact settings of these four angles for a given lesion can then be set in two ways. The arc guidance system can be set on a phantom base and the angles adjusted so that a probe inserted through the probe holder just touches the phantom target. The depth of the probe is measured and the arc settings are locked down. The arc is then transferred to the patient and attached to the head ring. The probe is inserted to the measured depth Alternatively the four angles can be calculated if the coordinates of the entry and target points are known.

The first **arc radius frame system** developed by Lars Leksell is one of the most popular stereotactic devices in the world. This apparatus comprises a semicircular arc on which a probe carrier is mounted such that it always points to the center coincides with the intracranial target. Thus a probe equal in length to the radius of the arc will hit the target The arc can be pivoted 180 degree anteroposteriorly and the probe holder may be translated along the arc in the frontal plane The chief benefits of this kind of system is that trajectories can be selected without the need to modify the arc settings or the depth. Other arc radius frame systems currently in use including the CRW (Cosman – Roberts-Wells),Laitinen, Patil, Olivier-Bertand-Talairach, and Zamorano-Dujovny frames.

Leksell G frame currently available can be used interchangeably with all available imaging tools The frame consists of a rectangular base ring 190 >< 210 mm The x coordinate is set on the semicircular arc which is attached to the frame at the chose y and z coordinates Either a straight front piece or an interchangeable front piece that accommodates the nose is used The x,y, and z axes of the coordinate system frame are similar to the x ,y and z geometry of CT, MRI An imaginary frame origin (x,y,and z=0)is at the superior posterior and right corner of the frame. A variety of fiducial systems are available for imaging registration. Working distance of most probes is 190mm, which is the radius of semicircular arc. When the probe stop on the instrument carrier is set at zero, the tip of probe will reach the target with an accuracy of <1mm The accuracy of reproducibility and precision of stereotactic targeting using the Leksell system meets the guidelines established by the American Society for Testing and Manufacturing.

Focal point systems use the arc radius construction with an important distinction. Instead of bringing the impact point to the target by changing the position of the arc relative to the frame the target is brought to the impact point by moving the patients head to the center of the fixed arc. Examples of this kind of system include Todd-Wells frame and the Kelly Goerss modification of that system. All current radio surgical devices presently available use a focal point construction.





STEREOTACTIC BIOPSY FOR INTRACRANIAL LESIONS

The realization that stereotactic surgery could be useful for the management of intracranial mass lesions evolved slowly. Clarke had suggested that stereotactic technique might be useful in the treatment of deep seated brain tumors in 1920 (Kelly, 1991) The possibility of stereotactic aspiration of cystic lesions was also mentioned by Spiegel et al in 1947 (Spiegel, 1947) In 1953 Talairach used stereotaxy for implanting radioactive sources into brain tumors (Kelly 1991) However the use of stereotactic biopsies to establish the histological diagnosis of an intracranial tumor was described much later. Surgeons initially believed that if they could find a tumor they might as well try to remove it and thus performed internal decompression Considering that in preCT era tumors were usually relatively large when the patients presented for surgery, this belief was justifiable Kalyan- Raman and Gillingham (kalyan-raman, 1964) also performed stereotactic biopsies as a means of confirming subcortical targets and they described a special biopsy needle. Backlund developed and described an instrument specific for brain tumor biopsy (Backlund 1974) In literature the first reported stereotactic biopsy of intraaxial tumors did not appear till 1973 when Conway reported a series of 31 patients comprising 16 pituitary adenomas, five pinealomas and 10 gliomas who underwent stereotactic biopsy. Specimens were obtained by needle or special biopsy forceps, non diagnostic tissue was obtained in three patients There were no apparent complications (Conway 1976)

Stereotactic biopsy is the simplest of all stereotactic procedures. The primary goal of a stereotactic biopsy is to obtain a tissue diagnosis. In some lesions this can be obtained form a single specimen. However in glial neoplasm's it is best to provide the pathologist with multiple specimens from various points within the tumor for accurate classification of the neoplasm into histological subtype and for grading. A stereotactic biopsy procedure also can establish the histological limits of a neoplasm. Hence a surgeon can determine where tumor ends and brain specimens from normal and abnormal areas obtained.

STEREOTACTIC APPROACHES

DATA REQUIREMENTS

In order to obtain as much information from a stereotactic biopsy procedure as possible it is best in planning the surgery to utilize as much preoperative imaging information about the tumor as is available. Preoperative imaging studies establish the location and limits of the lesion in stereotactic space and establish the position of important normal structures that should be avoided by the instruments. Stereoscopic angiography or MRI and position of surface and deep arterial and venous structures will be extremely important in planning a safe biopsy trajectory.

DATA ACQUISTION

Patient undergoes CT examinations with head fixed in the stereotactic head holder. In obtaining the CT and MRI data the entire lesion should be included within the limits of the examination in order to provide as many biopsies and trajectory options as possible in addition the Stereotactic arteriogram should include all vessels known to supply the area of the brain in which the lesion lies. For instance in planning a biopsy of a medial posterior temporal tumor both the ipsilateral carotid and vertebral arteries should be studied

SURGICAL PLANNING

Stereotactic frame coordinates may be derived for the target point within the tumor by utilizing several methods

T2 weighted MR image in glial neoplasms almost always demonstrates a more extensive lesion than is evident A question therefore arises as to which modality CT or MRI is best for target slice selection Where is diagnostic tissue most likely to be obtained?

Prudent target selection is critical to success of any biopsy. Diagnostic tumor tissue is always obtained from the contrast enhancing portion of most lesions on CT scanning This corresponds to gadolinium DPTA enhancement in T1 weighted MR images also. The T2 weighted sequence of the MRI on the other hand is useful in planning the extent of biopsy sampling in a serial trajectory within a glial neoplasm Therefore in general a target point is selected from the representative CT slice in the geographic center of a uniformly enhancing lesion or from the contrast enhancing ring in a lesion having a hypodense center. In hypodense lesions that do not exhibit contrast enhancement the center of the CT defined hypodensity is selected as the target point The stereotactic MRI is used to determine where the first and last biopsy samples should be obtained in a serial biopsy examination of certain glial neoplasms However several other factors should be considered in the selection of a target point for stereotactic biopsy Although the stereotactic system permits biopsy samples to be obtained with an accuracy of +/- 600 microns it is not wise to select a biopsy site very close to a known vascular structure if this can be avoided. In addition target points away from important neuronal structures are preferred if diagnostic tissue can be obtained just as easily as in a less critical location. In choosing the target point it is also necessary to know the mechanical limits of one's stereotactic frame For instance some stereotactic instruments have difficulty accessing far lateral or extreme anterior or posterior target points. In this situation it is preferable to choose a target point that lies on the medial side of a laterally situated lesion or on the posterior or anterior aspect of anteriorly or posteriorly located lesions, respectively.

Trajectory planning is an important step in stereotactic Neurosurgery. It is essential that the trajectory be safe and one that avoids major cortical vessels and areas of eloquent cortex. In general an entry point within watershed zone between the anterior and middle cerebral artery anteriorly or the posterior and middle cerebral arteries posteriorly is considered safe. This zone is usually centered 3 cm off midline at the level of coronal suture or 1-2 cm anterior to it. It is chosen because of the paucity of draining veins in this area. Regardless of the point of cranial penetration the risk of hemorrhage may be decreased by preoperative angiograms and minimized by preoperative stereoangiography The trajectory or probe tract will usually pass through white matter the blunt probe tip tending to push the axons aside rather then transecting them This minimizes the amount of neural injury.

In general burr holes or larger openings allow the escape of CSF and entry of air that can be associated with a shift of intracranial structures including the target within stereotactic space This may lead to suboptimal probe placement A small twist drill minimizes the CSF leak and may prevent such an occurrence.

Trajectory planning involves either an entry point method or an angles of entry method. The **entry point technique** involves choosing a location on the scalp that overlies a relatively avascular area of expanding cortex. The target point will have already been defined in 3 dimensional stereotactic space as described previously The target and entry points will define a straight line trajectory

On the other hand the **angles of entry technique** is particularly useful when operating on a superficial lesion. Misplacing an entry point even slightly may make the trajectory almost tangential to the skull. In this case the twist drill trajectory may deflect the probe off course and the twist drill or burr hole will need to be enlarged in order for the probe to pass to the target. The angle of entry technique tends to prevent this problem. This technique can be utilized with either the arc radius or polar coordinate system. In an arc radius system type of instrument, AP and lateral angles are used to construct the trajectory, some polar coordinate systems use AP and lateral entry angles, others use horizontal –Azimuth and Vertical-Declination angle of entry.

Ulm et al 2001 have used a new modern computer technology and neuronavigation for mapping the trajectory to the target from a chosen entry point on the surface. The computer does this preoperatively. Image fusion software is used for MRI scan to align MRI and CT database. AN operating room graphics is used and once the target and the entry point are chosen the workstation generates a theoretical needle trajectory between the points. The operator can view the trajectory on the CT or MRI images in coronal, sagittal, axial views or probe cross section view and if the trajectory crosses vital structures the entry point is changed till a satisfactory trajectory is obtained

PRINCIPLES FOR SUCCESSFUL STEREOTACTIC BIOPSY

The principles of stereotactic biopsy includes

→An aim not to cross more than one pial surface so that risk of haemorrhage is reduced to a minimum.

→Eloquent areas are avoided as far as possible to reduce postoperative neurological deficits.

→A track through ventricles is also avoided to minimize the risk of hemorrhage.

Other suggested principles for performing a successful stereotactic biopsy are listed in the table

General anesthesia
Head frame placement in children and adolescents
Burr hole placement
Burr hole placement
Allows direct visual inspection of the cortex
Cerebellar lesions
Superficial temporal and parietal lesions
Pontine lesions
Twist drill craniostomy
Transfrontal approach
Occipital approach
Biopsy trajectories
Transfrontal approach (preferred)
Transcortical approach for superficial lesions
Parietal approach for pontine lesions
Occipital approach for medial and posterior temporal lesions
Transcerebellar approach
Biopsy instruments
Side aspirating biopsy needle (preferred)
Corkscrew biopsy needle
Biting forceps

BIOPSY INSTRUMENTS

Stereotactic biopsies may be obtained using a variety of instruments The three most popular of these instruments and the methods by which they are used are described

1) BIOPSY CUP FORCEPS

The 1mm cup biopsy forceps were adapted form pediatric bronchoscopy forceps. These are inserted through a stereotactically directed cannula.

In practice the biopsy forceps is inserted in the closed position, opened, and rotated 90 degrees. The cups of the forceps are then closed and the forceps withdrawn slowly and carefully back into the cannula. Resistance to withdrawal of the forceps may indicate that it has grasped a blood vessel. In this event the forceps should be advanced to the biopsy position, opened, rotated 90 degrees closed carefully and withdrawn. Then the cannula should be irrigated with saline to ensure that no bleeding has occurred. The stylet is inserted, the cannula is advanced 3 to 5 mm and a biopsy is attempted at this level.

The major disadvantage of the cup biopsy forceps is that the biopsy specimens obtained from them are usually small typically up to 1.5mm in diameter. This does not provide much tissue for special stains and electron microscopy if these are necessary. However two or three additional specimens can be obtained at each biopsy site by simply rotating the biopsy cup to a different angle before taking each specimen. Typically biopsies are obtained in four quadrants 0,90,180,270 degrees relative to the vertical plane.

The advantage of biopsy cup forceps is that the surgeon has some tactile feedback when withdrawing the forceps and with experience can usually determine if a vessel is caught within the cup.

2) Backlund Instrument

A corkscrew biopsy instrument was originally described by Backlund. This instrument is also inserted into a stereotactically placed cannula and advanced to within 1 cm of the end of the cannula. It is then rotated clockwise until the instrument is fully inserted. This action corkscrews a specimen, which is then carefully withdrawn back through the cannula. Resistance encountered in the early withdrawal phase again may indicate a blood vessel entrapped by or coursing through the corkscrew. This situation can be salvaged by rotating the instrument counterclockwise in order to back off the corkscrew and thereby free the vessel.

The Backlund instrument usually obtains an adequate biopsy specimen typically 1 cm long by 1 mm in diameter. However its main theoretical disadvantage stems from failure to recognize an entrapped blood vessel in the corkscrew as the specimen is being withdrawn. In this instance not only may the vessel be injured at the biopsy site it could also be avulsed from its parent vessel

3) Side window cannula

This instrument was originally described by Sedan et al. and has been used extensively. It consists of an inner and an outer cannula each containing a 10mm long side window. Rotation of the inner cannula with respect to the outer cannula lines up these two windows or closes them. Aligning marks on the shafts of the inner and outer cannulas indicate that the window is open or closed. A leurlock syringes adapter is fitted onto the end of the inner cannula. An air lock or “O” ring over the proximal end of the outer cannulas when a vacuum is applied by means of a syringe. Finally a stylet is inserted into the inner cannula when the biopsy cannula is advanced.

The side biting window cannula is used as follows. The instrument with the sylet inserted and window closed is advanced to the desired stereotactic position. The stylet is removed and the inner cannula is rotated to align the window apertures of the inner and outer cannulas. A 12 cc syringe is then applied to the syringe adaptor and approx 1 to 2cc of suction is applied with syringe. This draws tissue into the window. While maintaining the suction the surgeon rotates the inner cannula so that the windows no longer align. This closes the window and amputates the biopsy specimen from the parenchyma The “O “ ring adaptor is then loosened to relieve the vacuum and the inner cannula is slowly withdrawn. This method typically withdraws a specimen 1 cm in length and 1.5mm in diameter. This is adequate for routine histological examination special stains electron microscopy and research studies Additional specimens can obtained at any biopsy position by rotating the cannula so that window faces in another direction

There are two disadvantages of this instrument. First it retrieves a large specimen. In infiltrating gliomas this large specimen may contain intact functional parenchyma and minor usually transient neurological deficit can result. Second there is no tactile way for a surgeon to know if a blood vessel has been drawn into the cannula window before rotating the inner cannula and amputating it Thus the risk of hemorrhage with this instrument is somewhat higher than with the biopsy forceps.

STEREOTACTIC BIOPSIES: PATHOLOGICAL CONSIDRATIONS

Smears and frozen sections are used for rapid intraoperative analysis of Stereotactic biopsies.

The smear technique was introduced in the 1930 by Cushing and Eisenhardt, then refined by Russel and remains widely used. Smears have become central to intraoperative diagnosis.

They offer a number of advantages.

1) They consume little of the precious tissue available from an stereotactic biopsy
2) They are easy to prepare requiring little time and no equipment
3) They can be made without risk of contaminating microtomes in cases of suspected or unsuspected organisms such as HIV, hepatitis B and C, or mycobacteria
4) Most importantly they afford the best analysis of the cellular composition of a lesion.

Smears are made from suspicious areas of the biopsy sample. Approximately 1mm tissue particle is pressed between two slides then evenly spread between them. Following brief fixation in 95% alcohol most pathologists stain smears with hematoxylin and eosin or hemalum and phyloxine and occasionally with special stains such as Wright Giemsa or toludine blue.

Smears can provide useful information about the way cells associate, cellular features and parenchymal characteristics of a lesion The degree of cell adhesion to other tumor cells or blood vessels provides critical clues about the tumors identity. Tumor cells from carcinomas, meningiomas and craniopharyngiomas that have adhesive membrane specialization tend to smear as clumps or sheets. Tumor cells without them such as those form astrocytomas oligodendrogliomas, lymphomas and inflammatory cells like macrophages smear out as individual dissociated cells. Cell association with blood vessels as seen in ependymomas or choroid plexus papillomas produces perivascular pseudorosettes or papillary like structures Even the degree of cohesion may be helpful in cases in which the differential diagnosis is low grade astrocytoma versus reactive astrocytosis because reactive cells tend to smear as clumps.

Cytoplasmic features are also better evaluated on smear than on frozen sections. For example in cases in which a primary CNS glioma is suspected, the presence and nature of glial processes facilitate differentiation between astrocytic, oligodendroglial, and ependymal tumors. For cerebellopontine angle tumors, the presence of elongated, spindled processes may distinguish a nerve sheath tumor from many but not all types of meningioma.

Nuclear size, shape, chromatin pattern and inclusions are also assessed better on smears, which are not subject to the distortions of freezing artifact. In cases in which a primary glioma is suspected, nuclear elongation and angulations help to distinguish neoplastic astrocytes form rounder oligodendrocyte nuclei. For extraaxial tumors, large, elongate club shaped nuclei may suggest a nerve sheath tumor, thin smaller elongated nuclei suggest a fibroblastic meningioma.

Noncellular background features may also provide clues to diagnoses. For example the presence of hemosiderin in smear from a spindle cell lesion of the cerebellopontine angle would suggest a diagnosis of schwannoma. Schwannoma exhibit intraparenchymal hemorrhage more commonly than many spindle cell tumors such a s fibroblastic meningiomas occurring at that site

The diagnostic accuracy of smears has been extensively reviewed and ranges from 87 to 94%, proving particularly effective in identifying the presence of a primary or metastatic tumor. Nevertheless such a limited analysis is fraught with pitfalls. These are mainly due to the small number of cells evaluated by smears relative to the entire sample or from smearing a portion of the biopsy that is unrepresentative or comes from an area of reactive gliosis around a lesion. Diagnostic difficulties were most commonly encountered in distinguishing between reactive astrocytosis and low-grade astrocytomas. Smears inadvertently made from a portion of the biopsy adjacent to a lesion may be particularly misleading. Poorly prepared smears that are too thick may exaggerate the degree of astrocytic cellularity and further confound the analysis. Preparation of smears from several parts of the sample usually reduces the chance of making a diagnosis based on unrepresentative tissue.

Frozen sections are made by placing select fragments of biopsy tissue in mounting medium on metal platforms, then rapidly freezing the tissue in cold isopentane or liquid nitrogen. Thin 5-10um sections are cut in microtomes cooled to –20 C then rapidly stained usually with hematoxylin and eosin.

In contrast to smear, frozen sections afford a more extensive evaluation of the tissue and valuable information about the cellularity and architecture or organization of cells in a lesion. For this reason many institutions still rely heavily on these technique for introoperative diagnosis. Standard 5um sections often reveal the degree of cellularity more accurately than smears. In addition sections afford a search for structures of diagnostic value such as neovascularity and endothelial proliferation, pseudopalisading, necrosis fibrinoid necrosis of blood vessels, ependymal rosettes and glandular formation

Diagnostic accuracy of frozen section alone appears to be about 90%. In combination with smears, its value seems to be enhanced. To accommodate this neurosurgeons typically submit two biopsies from the target site, designating one for immediate intraoperative evaluation and the other for permanent section. Nonetheless, in cases of extremely small samples, the potential loss of diagnostic tissue may outweigh the value of definitive intraoperative diagnosis, particularly when such information does not influence the operative plan.

POSTOPERATIVCE ANALYSIS OF BIOPSIES

Final analysis of biopsy samples involves consideration of clinical neuroradiological and tissue changes of a lesion. In addition to histological analysis, samples can now be analyzed by special stains, immunohistochemistry, electron microscopy and flow cytometry. Current molecular biological techniques such as in situ hybridization and polymerase chain reaction facilitate identification of specific characteristics of tumors or infectious agents.

CONSIDERATIONS DURING PATHOLOGICAL ANALYSIS

A) *GRADING AND CLASSIFICATION OF GLIOMAS*

Histological heterogeneity of anaplastic astrocytomas and glioblastomas presents special problems for neuropathologists and neurosurgeons alike. Diagnosis will reflect the grades of tumor in the areas sampled rather than the highest grade of the tumor. Sampling of nonenhancing central areas may deliver only nondiagnostic necrotic debris that could also be seen in an abscess or infarction. Biopsies at the perimeter may deliver only brain containing isolated infiltrating tumor cells rather than representative tumor. Thus small biopsies of tumor may be undergraded. In an effort to minimize diagnostic errors inherent to small samples, Daumas Duport has devised a new scheme for grading fibrillary astrocytomas that is less dependent of specific features such as the presence of necrosis.

According to Dumas Duport scheme four parameters are used to define degree of malignancy namely nuclear abnormalities, mitosis, necrosis and vascular endothelial proliferation.

None of the features- Grade 1

Presence of one parameter- Grade 2

Presence of two parameters- Grade 3

Presence of three parameters- Grade 4

B) *OLIGOASTROCYTOMAS AND EPENDYMOMAS*

Accurate diagnosis of such tumors is dependent on adequate sampling of both histological types and careful microscopic analysis. Similarly many areas in ependymomas and subependymomas exhibit a fibrillary background and nuclei suggestive of astrocytomas. Biopsies of fibrillary areas devoid of ependymal features such as perivascular pseudorosettes might mislead one to a diagnosis of astrocytoma.

C) ANAPLASTIC OLIGODENDROGLIOMAS

As oligodendrogliomas dedifferentiates, many tumor cells acquire astrocytic differentiation and resemble gemistocytic astrocyes. They can comprise a sizable proportion of anaplastic oligodendroglioma. Biopsies of these areas reveal tumor that the unwary might classify as gemsitocytic or anaplastic astroctyoma. Recent studies suggest anaplastic oligodendrogliomas may respond to procarbazine, cyclophosphamide and vincristine therapy making this distinction increasingly important.

D) TUMORS MIMICKING OLIGODENDROGLIOMAS

Pilocytic astrocytomas, clear cell ependymomas, neurocytomas, and dysembryoplastic neuroepithelial tumors can mimic oligodendrogliomas. Lack of infiltration, location and more classic areas containing pseudorosettes and ultra structural features suggest the diagnosis of ependymoma. Intraventricular location in the anterior lateral ventricle attachment to the septum pellucidum and the presence of anuclear fibirillary zones all suggest the diagnosis of central neurocytoma. Young age of the patient, a long-standing history of partial complex seizures, temporal or parietal lobe, and intracortical location suggest the diagnosis of DNT.

E) RESIDUAL GLIOMA AND RADIATION EFFECTS

Radiation therapy often produces a heterogeneous pattern of necrosis and reactive astrocytosis, which may be difficult to distinguish from residual tumor, especially because post irradiated tumor may appear hypocellular. In most cases radiation induced atypia in parenchymal astrocytes exhibits vesiculation of the nucleus, prominent nucleoli, and bizarre configurations of cytoplasm that readily distinguish parenchymal astrocytes from neoplastic astrocytes with hyperchromatic nuclei. Likewise zones of radiation induced coagulative necrosis can be distinguished from residual tumor with hypercellular foci pseudo-palisading around necrosis. Unfortunately in most cases due to treatment the tumor hypercellularity may be absent and intermingling of reactive and anaplastic astrocytes may preclude certain diagnosis.

F) GLIOBLASTOMA VERSUS ABSCESS

In GBM large zones of coagulative necrosis may be accompanied by neutrophils, producing a histological picture reminiscent of an abscess. Biopsies of these areas in isolation may suggest a diagnosis of brain abscess in a peripherally enhancing solitary lesion. In adequately biopsied tumors other samples will reveal the neoplastic nature of the lesion.

G) REACTIVE GLIOSIS AROUND TUMOR

Severe reactive gliosis mimicking an astrocytoma may accompany other primary CNS tumors, particularly hemangioblastomas, cranio-pharyngiomas and primary CNS lymphomas. Existence of Rosenthal fibers typically present in gliotic areas around these tumors may be particularly misleading. Nonetheless recognition of reactive features such as nuclei with prominent nucleoli and elongated fiber processes in these astrocytes usually suggests the correct diagnosis. Morever additional biopsies from other areas may deliver definite tumor tissue.

H) GRANULOMATOUS INFLAMMATION AROUND TUMORS

Germinomas commonly elicit a granulomatous reaction at their periphery, which in isolation is indistinguishable from granulomatous reaction associated with infections or sarcoidosis. Inadvertent biopsy of these areas as tumor tissue will inevitably result in the wrong diagnosis. A high index of suspicion adequate sampling and communication between the neurosurgeon and pathologist will reduce the likelihood of this diagnostic pitfall.

I) TOXOPLASMA ABSCESS VERSUS LYMPHOMA

Ten percent of patients with acquired immunodeficiency syndrome will develop focal brain lesions. Most commonly these are toxoplasma abscesses or lymphomas, lesions that may be indistinguishable by CT and MRI scans. The promise of new treatments for both HIV and opportunistic infections increases the urgency of rapidly diagnosing brain lesions in patients with AIDS. Biopsies demonstrating only focal zones of necrosis, atypical lymphocytic infiltrates, and peripheral reactive astrocytes commonly encountered in both lesions can present a diagnostic challenge. Histological features such as a robust macrophagic infiltrate accompanied by small nontransformed lymphocytes suggest a diagnosis of toxoplasma abscess. Even in largely necrotic samples, the presence of limited collections of transformed lymphocytes and vascular changes should suggest the diagnosis of lymphoma. In either case ample sampling usually renders the correct diagnosis.

J) DEMYELINATING LESION MIMICKING GLIOMA

Subacute demyelinating plaques although typically arising in periventricular or deep white matter, can develop anywhere in the CNS They may produce neurological signs and neuroradiological abnormalities with peripheral enhancement and rapid radiological progression that are identical to those of brain tumors. Histological features particularly near the edge of plaques mimic gliomas because these areas are hypercellular and contain proliferating oligodendrocyte, oligodendrocyte like macrophages, numerous enlarge reactive astrocytes and capillary prominence Thus biopsies of subcaute plaques may be mistaken for gliomas particularly during intraoperative analysis of small sample Key to recognition of these lesion as plaque is identification of macrophages which are readily seen in low grade gliomas. The reactive nature of the astrocytes and evidence of demyelination provide additional clues that the lesion is demyelination rather than neoplastic Such features are usually revealed by multiple biopsies from the periphery and center of such lesions.

CONCLUSION:

Despite limited sampling and the attendant risk of receiving unrepresentative tissue, STB have proven to be reliable diagnostic tool. STB deliver sufficient tissue for an accurate diagnosis in 63 to 95% of cases. STB when skillfully performed and analyzed, provide accurate diagnosis in the majority of cases. Careful target selection, judicious intraoperative consultation, and cautious pathological interpretation can all enhance the diagnostic value of this procedure.

ROLE OF STEREOTACTIC BIOPSY

Patients who present with an intracerebral mass lesion, stereotactic biopsy may be used to establish a diagnosis. It may be followed by bulk resection if the diagnosis is of a primary brain tumour and is accessible, unless it is a midline tumour or a diffusely growing hemispherical lesion. STB is also used to establish a histological diagnosis in a patient with multiple intracranial lesions with a known primary elsewhere when metastasis is suspected. It is also included in the management protocol in patients with a known tumour elsewhere and have a single intracerebral mass lesion, with no other evidence of metastases elsewhere. It is essential to obtain a histological diagnosis, as the lesion may not always be a metastases. One of the options in management of low-grade gliomas is stereotactic biopsy and radiotherapy (Lunsford, 1995), though this controversial. There is still no Class I evidence, which conclusively proves that radical resection is associated with better outcome in low-grade gliomas. Aggressive resections are however advocated as it provides a longer progression free survival and the disease is treated when the neoplasm is smaller (Keles, 2001) but all options are theoretically acceptable.

Single small CT lesions, which are enhancing are not always tuberculomas and have been found to be cysticercal granulomas on stereotactic biopsy (Chandy, 1991). No imaging picture is diagnostic of tuberculomas as other lesions on CT scan can mimic tuberculomas Stereotactic biopsy provides a definitive histological diagnosis in 45% but the inflammatory nature of the mass is confirmed in 100% of cases, thus excluding a neoplastic process (Ranjan 1993, Rajshekhar 1990).

Forsyth et al (1995) used stereotactic biopsy in differentiating radiation necrosis or glioma recurrence in 51 patients with supratentorial gliomas treated with external beam radiotherapy. They showed recurrence in 59%, radiation necrosis in 6% and mixture in 33%, and radiation induced tumour in one. They thus proposed that stereotactic biopsy could be used to differentiate tumour recurrence, radiation necrosis or radiation induced neoplasm (Forsyth, 1995)

A landmark study by Chandrasoma et al analyzed the accuracy of image guided stereotactic brain surgery in 30 patients who had mass lesions of the brain and subsequently underwent resection of the mass. The histological diagnosis at stereotactic biopsy was appropriate for further clinical management in 28 of 30 patients. It was not accurate in 2 patients only (5% non diagnostic) one of them had GBM where the biopsy showed necrotic tissue. The second patient with pineal germinoma was found to have large areas of granulomatous inflammation in the biopsy. They concluded that with accurate target point placement, the biopsy sample can be representative enough of the entire lesion to enable clinical decision to be made (Chandrasoma, 1989)

Bullard et al reported a positivity rate of 64% in an initial report of stereotactic biopsy results. Heilbrun et al in 1983 reported a positivity rate of 45% in 11 cases in a preliminary report with BRW frame. Hood et al reported a positivity rate for stereotactic biopsy of intrinsic lesion of brain stem in 12 patients in 1986. In a large series of 500 cases in 1987 Apuzzo et al published a positivity rate of 95.6% using the BRW frame Kelly et al similarly obtained a positivity rate of 98% in a series of 543 stereotactic biopsies. In a study from Vellore, India the positivity rate was 92.8% amongst 431 biopsies using CRW stereotactic frame. Hall reported a positive biopsy rate of 96% in 134 Biopsies. In a recent study from University of Florida Ellis reported 96% with stereotactic biopsy. With more and more experience in stereotactic biopsies, the positivity yield rate has improved from an initial 64% to 98% Using advanced neuronavigational technique in 200 consecutive stereotactic biopsies a positivity rate of 98.5% was obtained. (Ulm 2001)

The expectations from stereotactic biopsy for non-neoplastic lesion are far less and in most cases the smear shows reactive gliosis and inflammatory cells. In approximately 20 percent of cases with reactive gliosis and inflammation, a specific diagnosis can be made (Chandy, 1996) Diagnosis would be possible in cases in which there are numerous foamy macrophages in the clinical setting consistent with cerebral infarction and cases in which a specific infectious agent is identified in the biopsy. Infections encountered include tuberculosis, fungal infections, cysticercosis, herpes simplex and cytomegalvirus encephalitis, progressive multifocal leucoencephalopathy and toxoplasmosis. Electron microscopy may demonstrate unspecified viral particles, providing for evidence of viral encephalitis. If tissue remains after processing it can be used for mycobacterial fungal or viral cultures. Patients with a stereotactic biopsy diagnosis of reactive gliosis and inflammation are carefully followed up and a repeat biopsy is done when clinically indicated. It is uncommon for these cases to be neoplastic.

CONTRAINDICATIONS FOR STEREOTACTIC BIOPSY

Stereotactic biopsy is not indicated when vascular lesion is suspected on neuroradiology studies as biopsy can precipitate hemorrhage from the tumor vessels. In lesions that have a significant mass effect with midline shift, biopsy although can be tolerated, a small hemorrhage or edema, complicating the instrumentation could theoretically result in neurological decompensation and herniation.

COMPLICATIONS

Mortality rates after stereotactic biopsy is reported to be in the range of 0.6% to 3% and the procedure related morbidity has been reported between 1% to 5.9% (Lunsford 1984, Greene 1989, Bernstein1994, Favre 2002) The risk factors for operative complication from stereotactic biopsy are surgical experience, histology, location of tumour and presence of increased intracranial pressure. Malignant lesions with neovascularisation and abnormal vessel structure, such as malignant glioma and lymphoma are more prone to bleed and produce edema following blind manipulation. Regarding location, biopsy of brain stem lesions and those in eloquent cortex might be expected to be more prone to result in neurological deterioration. The likely increase in perilesional edema following needle biopsy, as well as the actual volume of the inserted biopsy device could combine to precipitate a decrease in function of neurons or white matter tracks Bernstein, 1994).

HEMORRHAGE AND ITS MANAGEMENT

Intracranial hemorrhage can result from injury to normal blood vessels or tumor vessels. Pulsatile flow of arterial blood out of the biopsy cannula indicates arterial injury. Venous bleeding is noted by slow ooze. If arterial or venous bleeding is noted following withdrawal of the biopsy specimen it is important not to move the biopsy cannula. A hematoma will not form intracranially as long as there is a clear path of low resistance for blood to flow out of the cannula. The cannula should periodically be irrigated with a stream of saline from a blunt tipped needle and syringe to dislodge clot from the cannula and keep the route open for egress of blood. When the bleeding stops, it is important to be sure that it has not stopped because of a clot having formed in the cannula otherwise an intracranial hematoma could form. It is therefore necessary to keep the cannula open. If the cannula cannot be cleared with an irrigating stream of saline the next step is to replace the stylet and remove it again. Also an extra long suction tip that fits down the cannula can be used to extract a clot from it. The surgeon can safely assume that the bleeding has stopped after having placed and removed the stylet and after having irrigated the inside of the cannula and received only clear irritant in return. It is important to be patient. If the biopsy trajectory was planned carefully in order to avoid intracranial vessels, visualized on stereotactic angiography, bleeding must be from tumor vessels. Tumor vessel bleeding eventually stops unless it adjoins ventricular system or subarachnoid space where blood mixes with and is carried away by the cerebrospinal fluid and does not come out the biopsy cannula. There is not much that can be done except prevent hypertension by the administration of liberally or nitroprusside. Bleeding coming out the biopsy cannula should stop within 20 minutes. If it has not stopped after 20 minutes a stereotactic craniotomy to coagulate the bleeding point should be considered.

SEIZURE

Brain overlying subcortical tumors particularly low grade astrocytomas and oligodendrogliomas is usually irritable. Passing a probe through the subcortical tissue can provoke a seizure inspite of adequate anticonvulsants. If a seizure does occur with the biopsy robe in place, the probe should be removed immediately. The surgeon should abort the procedure and proceed later with the patient placed under general anesthesia.

INFECTIONS

Superficial infections at the entry site of the biopsy cannula are rare. They respond favorably to appropriate antibiotic. Intracranial abscess following stereotactic biopsy is also very rare. Treated by stereotactic aspiration and appropriate parenteral antibiotic.

Materials and methods

This study was conducted retrospectively as well as prospectively. Case records of patients who underwent stereotactic biopsy from August 1998 to June 2003 at Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST) were analyzed. The indication for biopsy was

1. deep seated lesion which were not accessible by conventional surgical methods
2. lesions located in eloquent areas
3. diffuse lesion
4. If a diagnosis of the lesion was in doubt with conventional neuroradiological studies.
5. Multiple Intracranial space occupying lesions

All patients underwent biopsy using Leksell G frame. Biopsy was performed either using CT/MRI guidance. MRI guided biopsy was considered if the lesion was ill defined on CT Scan or was visualized only on MRI imaging. The biopsies were done under local anesthesia in adults and under GA in children and uncooperative patients.

After frame fixation patient were shifted to CT scan room. Plain and contrast CT scan done for all the patients. An enhancing solid portion of the lesion was selected as target. Targeting the central necrotic part was avoided. Coordinates (X, Y, Z) were measured and patient was shifted to OT.

A burr hole was done in all cases. For most of the lesions precoronal burr hole was used. The location of the lesion in the preoperative neuroradiological evaluation was considered for deciding on the side of the burr hole so that a direct ipsilateral approach to the lesion could be performed. Care was taken to avoid transgressing ventricular cavity during the biopsy

During biopsy multiple samples were obtained from all the quadrants at "0"target and if required from "–5 "or "+5" target. Side window cannula was used to take all the biopsies.

Specimens were immediately sent for frozen report. Once tumour tissue has been confirmed no further specimens were taken. In case of no tumour tissue specimens were taken from other sites. All specimens were send for histopathological confirmation

All the patients were observed for 24 hours following STB in ICU for any complications. Patients were discharged very next day of biopsy unless otherwise indicated.

Routine Postoperative CT scan was not done. Only in patients who showed neurological deficits or had intraoperative bleeding underwent CT scan.

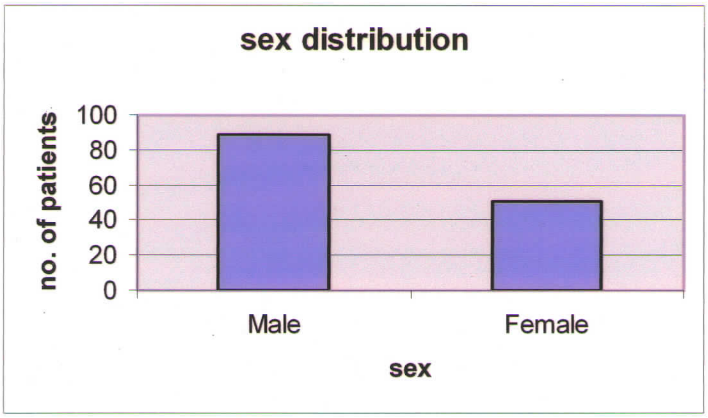
Patients with negative biopsy were given the option of repeat biopsy (under MRI) or follow up at regular intervals. Further management was instituted depending on the neuroradiological evaluation and follow up status of the patient.

Results and analysis

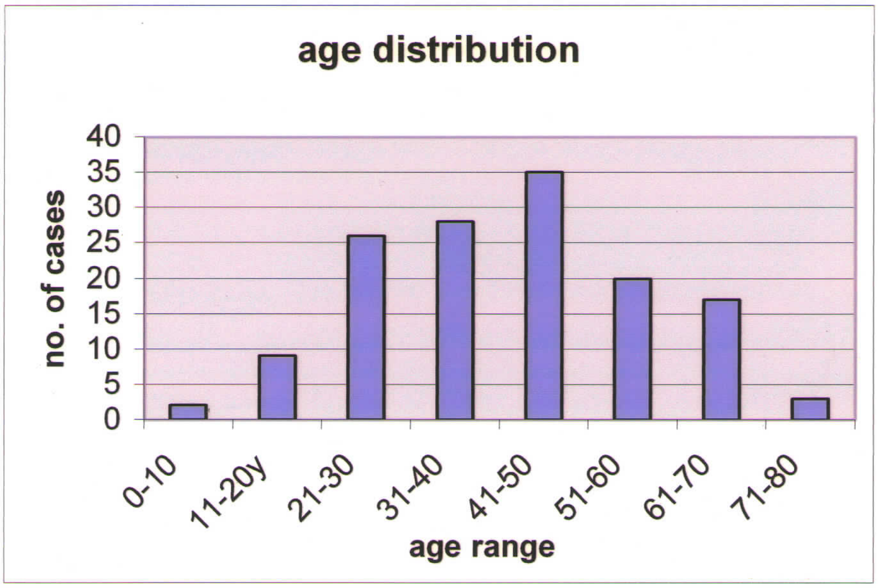
One hundred and forty patients underwent stereotactic biopsy between August 1998 to July 2003.

A. Sex distribution

Males were 89 and females were 51



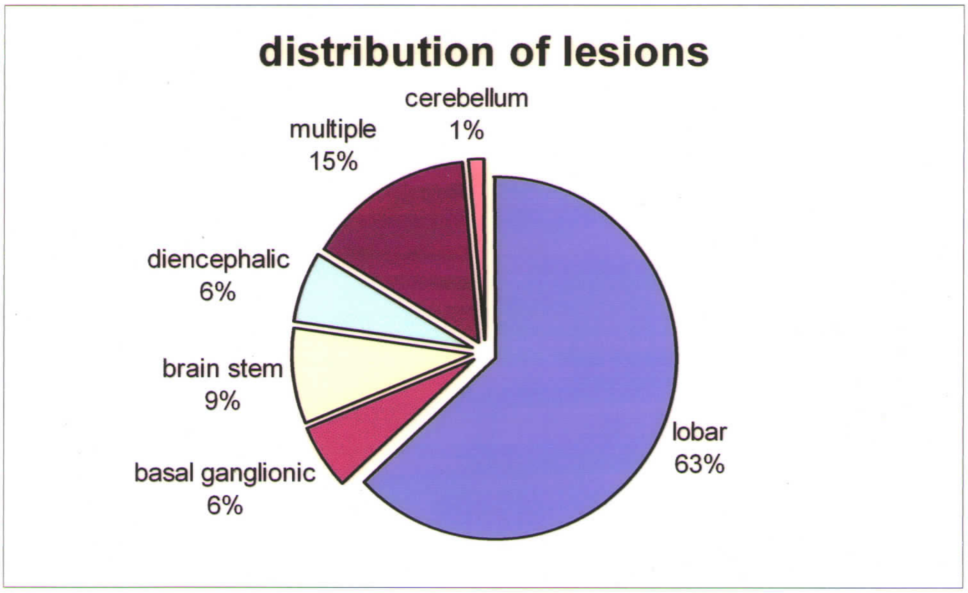
B. Age distribution



C. LOCATION

Based on the location of target lesion, lesions were divided into six categories: lobar, basal ganglionic, brainstem, diencephalic, multiple and cerebellum.

LOCATION	NO. OF PATIENTS (%)
LOBAR	88(63%)
BASAL GANGLIA	8(6%)
BRAIN STEM	12(9%)
MULTIPLE	21(15%)
DIENCEPHALIC	9(6%)
CEREBELLUM	2(1%)



D. Histopathology

Majority of the lesions were neoplastic. The commonest pathological lesion was glioma, majority being high-grade glioma. In 25 cases glioma grading could not be done. Out of 140 specimens, fourteen were inconclusive and in three cases adequate material for diagnosis could not be retrieved.

PATHOLOCAL DIAGNOSIS	NUMBER OF CASES
Low grade gliomas	24
High grade gliomas	40
Gliomas (not graded)	25
Metastasis	10
Lymphoma	7
Germinoma	1
Tuberculoma	5
Inflammatory pathology	4
Encephalitis	1
Infarct	2
Demyelination	3
Fungal granuloma	1
Inconclusive	14
Material not obtained	3
Total	140

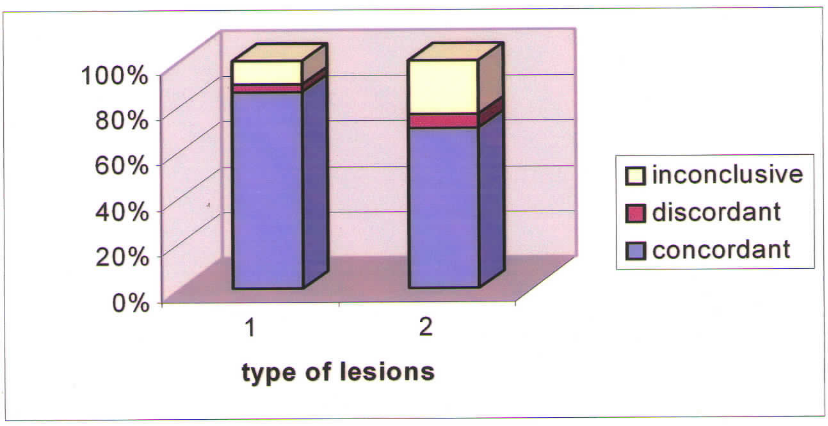
E. YIELD OF STEREOTACTIC BIOPSY

Out of 140 cases, based on radiological evidence 123 were neoplastic and 17 were non neoplastic pathology. Definite diagnosis could be reached in 123 cases. Thus yield of stereotactic biopsy was 88 %.

Out of 123 neoplastic lesions positive yield could be achieved in 110 cases i.e. 89.5%. 106 were neoplasms and 4 turned out to be nonneoplastic pathology. In this group 13 turned out to be inconclusive (10.5 %)

Out of 17 nonneoplastic lesions, positive yield could be achieved in 13 cases i.e. 76.5%. 12 were inflammatory lesions and 1 was diagnosed as neoplastic lesion. In this group four cases were inconclusive. (23.5%)

GROUP	NEOPLASTIC	NONNEOPLASTIC	TOTAL
TOTAL NO.	123	17	140
YIELD (%)	110 (89.5)	13(76.5)	123(88)
INCONCLUSIVE	13(10.5)	4(23.5)	17(12)
DISCORDANT	4	1	5



F. LOCATION AND YIELD

The yield rate from cerebellum was lowest as compared to other sites

LOCATION	NO. OF CASES	YIELD	YIELD RATE
LOBAR	88	81	92
BASAL GANGLIONIC	8	8	100
BRAIN STEM	12	11	91
DIENCEPHALIC	9	8	89
CEREBELLUM	2	1	50
MULTIPLE	21	14	66
TOTAL	140	123	88

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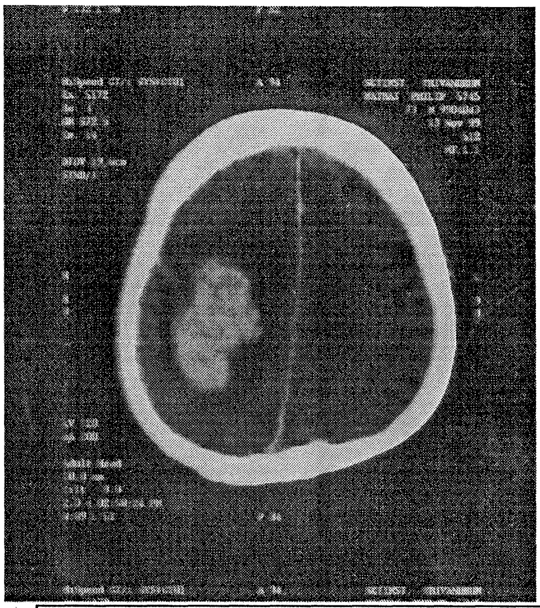
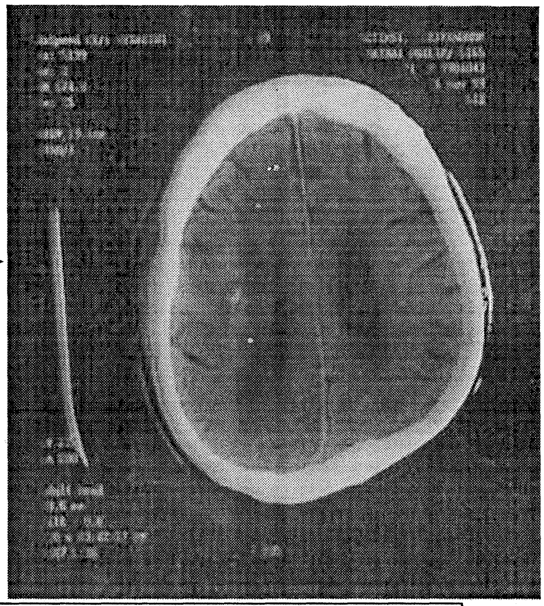
G. COMPLICATIONS

Few complications were encountered during this procedure. Most of them were minor and mainly bleeding, which could be controlled with saline wash. Major complications were very few. No mortality was present.

PRE OP IMAGE



POST OP IMAGE



COMPLICATIONS	
A. MINOR (n=8)	
1) Post or intra procedure seizure	3
2) CSF leak from wound	1
3) Transient hemiparesis	2
4) Transient 3rd nerve palsy	1
5) Small hematoma at operative site	1
B. MAJOR (n=2)	
1) Large hematoma at operative site	1(required evacuation)
2) Malignant brain edema	1

Bleeding from needle tract was encountered in six patients. Most of the them were controlled with saline wash. Two patients developed post op hematoma out of which one reqd immediate surgical evacuation. He improved after surgery. His histopathology was suggestive of metastasis.

Thus overall morbidity rate was 7 % and morbidity was zero percent.

Discussion

Although the ideal goal of all surgical procedures is complete removal of the lesion without precipitating any morbidity, the surgical judgement has to exercised in deciding the feasibility of resection as opposed to biopsies or sub total resection which the natural history of the presumed disease process together with the lesion size, location, infiltration to eloquent areas and extent.

Distribution of lesions: Brain stem and basal ganglia are traditionally considered to be locations, which are not reached by conventional surgical techniques. Lesions situated in these locations may vary from benign conditions like tuberculoma and cysticercosis granuloma to malignant lesions like anaplastic astrocytoma and glioblastoma multiforme. Stereotactic biopsies are a safe and minimally invasive method for attaining a histological diagnosis in lesion in these locations. Apuzzo et al performed 129 biopsies for diencephalic region and 5 from pontomedullary region out of 500 cases (Apuzzo, 1987). Ranjan et al performed biopsies from 87 deep ganglionic locations and 47 brain stem lesions in 600 procedures. (Ranjan, 1993). In present study biopsy was done for basal ganglionic lesions in 8 cases, brainstem in 12 cases and diencephalic in 9 cases.

Type of stereotactic frame: Various stereotactic frames have been used to obtain the stereotactic biopsies. Most of the conventionally used frames have been found to have an equal accuracy in several studies (Hall, 1999, Ellis 1999, Ranjan1998, Apuzzo, 1997 Heibrun, 1983). In several series the diagnostic yield using BRW frames have been between 87% to 96%. Similarly the positive rates with CRW have been 96%. In present series only Leksell G frame was used for biopsy.

CT or MRI Guidance? Stereotactic biopsies can be obtained either with CT or MRI guidance. With the advent of neuronavigational system biopsies can also be obtained with frameless stereotactic devices (ulm, 2001). CT can be used for biopsy of almost all intracranial masses, except those, which are ill defined. It has a relative disadvantage in imaging lesions in posterior fossa compared to MRI. MRI is useful in obtaining biopsy from lesion, which are ill defined on CT scan and lesions in the posterior. Both CT and MRI guided biopsy was done in the present study. All 17 inconclusive results were obtained when biopsy was done CT guided. All MRI guided biopsies were conclusive. One inconclusive biopsy after CT guidance was repeated under MRI guidance, which turned out to be conclusive. Thus statistically significant difference was found. MRI was found to be better reliable than CT scan.

Type of lesions: The term diagnostic yield is used rather than diagnostic accuracy because of the heterogeneity that exists within brain tumors and the small size of the tissue sample that are obtained with this technique. In this study malignant tumors represented the most frequent lesion biopsies. This compares favorably with other studies (Ranjan 1983, Hall 1998, Bosch 1980, Sedan 1984,Rajshekhar 1990) Various authors have reported that 15 percent of lesions in patients referred for diagnostic biopsy were nonneoplastic (O'Niell, 1992, Sedan 1984) In our series it was less than 10%.

Comparison of the histopathological diagnosis also reveals that gliomas are the most frequent histopathological finding followed by lymphoma and metastases. When a mass lesion is a neoplasm, a specific and accurate tissue diagnosis can be made in more than 90% of cases (Hall 1998,Bosch 1980,Blaauw 1998, Friedman 1989, Lunsford 1984) In this study it was evident in almost all cases except one case where nature of neoplasm could not be characterized.

Site of Biopsy: According to various series specimen is more likely diagnostic when an enhancing region of the mass is biopsied instead of the non-enhancing region. Most parenchymal neoplasms have infiltrating edges and a biopsy from this region is difficult to interpret and arrive at a diagnosis as it consists of normal brain reactive glial tissue, edema, neovascularity and neoplastic cells. Diagnosis is possible in cases of nonglial neoplasm such as metastatic carcinoma and is very difficult in cases of anaplastic glial neoplasm and almost impossible in cases of well differentiated glial neoplasm. If the biopsy is from and area where the neoplasm has completely replaced brain the diagnosis is much easier. Accurate targeting of the lesion and adequate sampling is considered essential to achieve a high diagnostic yield. In the present study biopsy yield from hemispheric lesions was 92%, while that from basal ganglionic was 100% and from Brainstem was 91%. Overall positive yield rate was 88% This compares favorably with other studies(Ranjan 1993,Hall 1998, Biosch 1980, Watanabe 1991, Apuzzo 1987, Ellis 1999,Hood, 1986). Heilbrun et al obtained 87% positive yield rate in 87 cases. They experienced failures when they targeted center of tumors with necrosis or when they encountered firm lesions (Heilbrun 1983). Hood et al obtained 100% results in 12 brainstem lesion after accurate targeting (Hoods 1986) Apuzzo et al experienced failures in 4%v of 500 cases they obtained non diagnostic biopsies as necrosis in 10 cases, inflammatory response in 9 cases, granuloma in 1 case failure to perforate a cyst as it was rubbery in consistency and inadequate sampling in a mixed tumor in one case each (Apuzzo, 1987) Ranjan et al obtained a 93&% result after targeting the contrast enhancing region of a lesion 600 cases and experienced difficulties in nonneoplastic lesions (Ranjan,1993).

In this series also positive yield for nonneoplastic lesions was low as compared to neoplastic lesions (76% vs. 89%). All the biopsies in this series were taken from the enhancing solid portion of the tumor. So no comparison between central and peripheral target is available. Hall et al and Ellis et al obtained a 96% positivity yield each and again experienced difficulties in inadequate or incorrect sampling in lesions with central necrosis, firm lesion and nonneoplastic lesions or if lesions were in proximity to the ventricular system (Hall 199 and Ellis 1999) One case in our series was periventricular and could not be targeted with CT guidance so was biopsied under MRI guidance and turned out to be positive. Ranjan et al in a series of 600 cases selected contrast enhancing region away from the ventricle of cisternal spaces and obtained a positive yield in 93% they obtained 3 to 4 bits for biopsy (Ranjan, 1993) Apuzzo et al selected multiple target sites for biopsy in a series of 500 biopsies and had a positive yield of 96% in their nondiagnostic cases 10 were necrosis as they had selected center of lesion, inadequate sampling was cited in inability to diagnose a mixed pineal lesion, They had administered double dose of contrast to ensure that they targeted contrast enhancing region of the tumor to obtain a high diagnostic yield (Apuzzo 1987) Heilbrun et a also utilized multiple targets in lesions with enhancing borders. They had a positive yield of 87% (Heilbrun 1983). In this series our protocol was to take biopsy until frozen shows evidence of definite tumor tissue. Not many complications were encountered in taking multiple biopsies except two patients who developed brain edema.

Frozen section Vs. formalin fixed Histopathological diagnosis

The handling of the biopsy material and the mode of analysis of the specimen have been classically by smear preparation to give the preliminary diagnosis and corroborate the adequacy of sample and accuracy of targeting. This however increases the operative time and the patient discomfort. In a study by O'Neil et al 259 biopsies in 245 patients were performed by 28 different surgeons. They did not use preoperative smear cytology in the firs 142 patients and obtained a yield of 86.6% but subsequently in 103 patients they used per operative smear cytology and improved their diagnostic yield to 94.2% (O'Neil, 1992). Fritsch et al in a series of 65 stereotactic biopsies had a 100% result and found no difference between the yield of frozen section and final diagnosis based on paraffin embedded sections (Fritsch, 1998) This also eliminates the need for routine squash smear examination in patients, in favor of formalin fixed paraffin examination. Routine paraffin sections of the stereotactic biopsy sample instead of squash smears maintain diagnostic accuracy with decrease in operation time and patient discomfort.

In this series frozen section was done in almost all cases except in few (3 cases) due to nonavailibility of cytopathologist. Eleven cases were reported inconclusive on frozen section. Five remained inconclusive even after HPR. Four turned out to be inflammatory lesion. One turned out to be demyelination and glioma each on definite HPR. Other cases were concordance between frozen and HPR was not found were as follows

FROZEN SECTION	HISTOPATHOLOGY
glioma	Encephalitis
Metastasis	Glioma(2 cases),
Tumour?nature	Glioma (3 cases) lymphoma(2 cases)
Inflammatory	Glioma (2 cases)
Granulomatous lesion	Infarct
Glioma	Lymphoma
Glioma	Normal brain tissue

Risk factors in stereotactic biopsies

Bernstein et al had a complication rate of 6.3% in 300 cases. In a Meta analysis of 5000 cases of stereotactic biopsies he noted a complication rate of 5%. They had a high complication rate for gliomas, lymphomas and metastasis in the range of 6.4%, 6.3% and 2.8% respectively. They also had a 12.5% incidence of morbidity in patients who were HIV positive (Bernstein, 1994). Favre et al observed no significant difference in overall complication in immunocompromised or non immunocompromised patients (Bernstein1994, Favre 2002) There were no immunocompromised patients in our series.

Tumors in pineal region are considered at a higher risk for bleeding during stereotactic biopsy than other locations (Favre, 2002). Regis et al reported mortality of 1.3% in multicentre study of 370 biopsies from pineal region (Regis 1996) Similarly brain stem lesions are also considered to be at an increased risk for developing complications, which has not be confirmed by recent series (Favre 2002,Bernstein 1994)

The risk factors have to be weighed against the benefits in stereotactic biopsies, especially of brain stem lesions. Rajshekhar et al have analysed 71 patients with brain stem lesions who underwent stereotactic procedures. They had a transient morbidity of 4.5% In patients suspected to have malignant lesions, a benign pathology was diagnosed in 9 cases, fluids from cystic masses could be aspirated providing benefit in six out of 8 cases, thus the procedure being beneficial for 13 patients. Other lesions such as demyelination, radiation necrosis, encephalitis and benign cyst adjacent to the brain stem may occasionally mimic a diffuse malignant glioma even on MR imaging (Rajshekhar, 1995) Hence a contrast MRI has to be performed before radiation therapy and for choosing patients for biopsy. As contrast MRI was not performed in Rajshekhar et al study, it is likely that some of the lesion could have been diagnosed in the MRI scan. It has been suggested that there is no role of biopsy for diffuse nonnenhancing brain stem masses in children diagnosed with MRI, as invariably these are malignant of gliomas with poor prognosis (Albright 1993)

Histology, location and presence of increased intracranial pressure are the most significant risk factor for the operative complications from stereotactic biopsy. Malignant lesion with neovascualrization, abnormal blood vessel are more prone to bleed and produce edema following biopsy. Biopsy of lesion in subependymal, subpial locations have a higher risk of bleeding and neurological deterioration. Patients with intracranial hypertension and decreased intracranial compliance are less able to absorb a small volume increment of intracranial contents as compared to patients with normal or mildly elevated ICP. Therefore a small increase in edema, a small hemorrhage and the volume of the biopsy device inserted into the brain could all precipitate transtentorial herniation. This was noted in three patients with resulting mortality in one study (Bernstein, 1994). In our series two patient developed brain edema with tentorial herniation. One was treated conservatively and one had to undergo temporal lobectomy.

Stereotactic biopsy is a widely used effective relatively low risk high yield procedure for determing the pathology of intraaxial brain lesion. With proper selection of patient for stereotactic biopsy, the target trajectory and biopsy device the incidence of complication can be significantly.

The ideal number of specimens required to obtain a positive diagnostic yield to minimize bleeding has not been established. A negative biopsy is preferred to negative outcome (Kondziolka, 1998). The type of lesion, its location associated disease, and experience of the neuropathologist dictates the number of specimens that should be obtained. Various studies published with multiple biopsies ranging from 2-6 specimens when the squash smear has been nondiagnostic did not show resultant increase in complications because of multiple biopsies (Hall 1999, Ellis 1999,Ranjan 1993 Apuzzo 1997, Hood 1986,Bernstein 1994,Favre 2002). The possibility that the number of biopsies may not add to the complication rate was put forth by Fritsch et al in a study of stereotactic biopsy of 65 intracranial brain lesion, They performed an average number of 13.8 biopsies with a median of 12.5, the minimum number being 1 and the maximum number being 48. They had an overall complication rate of 6.3% and a mortality of 1.7% (Fritsch, 1998)

To reduce the incidence of complications Gilsbach et al advocated the use of a new safety device the stereotactic Doppler sonography as an adjunct to prevent significant bleeding during stereotactic biopsy procedures (Gilsbach 1987) They used this device in 10 patients with difficult biopsies and to detect vessels is the neighborhood had no complication a the target point. The risk for developing symptomatic hemorrhage have been variously quoted from 0% to 40% (Kulkarni 1998,Moran 1979,Bernsein1994) The larger series of stereotactic biopsy, report complication in the range of 1.2-7.2% (bergstrom1976, Blauw 1988,Friedman 1989, Lunsford 1984, kondziolka 1995) Asymptomatic hemorrhage can only be detected only if a CT scan is obtained routinely after stereotactic biopsy sampling. Some have argued against the practice stating that it does not add significantly to patient management or outcome (kulkarni, 1998) In the present study 6 patients had bleeding from needle track four were controlled with saline wash. One patient had a small hematoma at operative site. One patient developed a large hematoma necessitating surgery for evacuation. We routinely don not perform CT scan postoperatively. Only patient with neurological deterioration underwent scan. There was no mortality in the present study. The reported mortality in the literature varies for 0-2.6% (Ranjan 1993,Hall 1998, Bosch 1980, Blauw 1988, Green 1989, Bernstein 1994, Kulkarni, 1998)

CONCLUSION

In the present study CT and MRI guided stereotactic biopsies with Leksell frame yielded a positive biopsy rate of 88%. Positive yield was more in neoplastic lesion than nonneoplastic lesions. Overall morbidity was 7% with zero mortality.

Thus stereotactic biopsy is an important tool in the neurosurgeon's armamentarium. It has high positive yield rate with low morbidity and mortality. Intracranial pathologies that are ideally managed with adjuvant therapy following histological verification like primary cerebral lymphomas, high grade gliomas, inflammatory masses. For such lesions STB is the ideal minimally invasive technique for obtaining diagnosis.

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