



بسم الله الرحمن الرحيم

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A Systematic Review: Diagnostic Accuracy and Complications of Endoscopic Versus Stereotactic Biopsy in the Management of Pineal Region Space Occupying Lesions.

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“It’s not the destination, it’s the journey.” *-Ralph Waldo Emerson.*

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List of Abbreviations

V. cerebel. Mes. Fiss.	Vein of cerebello-mesencephalic fissure
Med-post choroid. Art.	Medio-posterior choroidal artery
PCA	Posterior cerebral artery
SCA	Superior cerebellar artery
CSF	Cerebrospinal fluid
MRI	Magnetic resonance imaging
HCP	Hydrocephalus
ETV	Endoscopic third ventriculostomy
STX	Stereotaxy/Stereotaxic
SCN	Supra-chiasmatic nucleus
PVN	Para-ventricular nucleus
NE	Norepinephrine
AA-NAT	Arylalkylamine N-acetyltransferase
5HT	5-Hydroxytryptamine
NAS	N-Acetylserotonin
Bmal	Brain and muscle ARNT-like
CCG	Clock controlled genes
SCG	Superior cervical ganglion
RHT	Retino-hypothalamic-tract
MT	Melatonin receptors
PRC	Phase response curve
LH	Luteinizing hormone
FSH	Follicle stimulating hormone
T2DM	Type 2 diabetes mellitus
ASD	Autism spectrum disorder
GnRH	Gonadotropin-releasing hormone
DLMO	Dim light melatonin onset
CNS	Central nervous system
PNET	Primitive neuroectodermal tumors
GCTs	Germ cell tumors
NGGCTs	Non-germinomatous germ cell tumors
NSE	Neuron specific enolase
GFAP	Glial fibrillary Acidic protein
PXA	pleomorphic xanthoastrocytoma
ETB	Endoscopic tumor biopsy
PLAP	Placental alkaline phosphatase
STGC	Syncytiotrophoblastic germ cells
HCG	Human chorionic gonadotrophins
PAS	Periodic acid-schiff
CT	Computerized tomography
PET	Positron emission tomography
EVD	External ventricular drainage
VP	Ventriculo-peritoneal
RCT	Randomized control trial
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analysis

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***I*ntroduction**

Introduction

The pineal gland has always fascinated scientists, philosophers and writers alike. Perhaps due to its deep seated location and single “unpaired” nature, it was regarded as a "mystery" gland with mystical, metaphysical, and occult theories surrounding its perceived functions. Descartes, for instance, believed that it housed the soul and the place in which all our thoughts are formed.⁽¹⁾

The notion of a "pineal-eye" is central to the philosophy of the French writer Georges Bataille. Bataille uses the concept of a "pineal-eye" as a reference to a blind-spot in Western rationality, and an organ of excess and delirium.⁽²⁾ In the late 19th century Madame Blavatsky (who founded theosophy) identified the pineal gland with the Hindu concept of the third eye, or the Ajna chakra. This association is still popular today.⁽¹⁾ Even the Egyptian doctor and novelist Mustafa Mahmoud, perhaps influenced by Descartes, mentioned the pineal gland as a potential place of the soul.⁽³⁾

In the more modern understanding, the pineal gland is linked to regulation of the circadian rhythm and the onset of puberty through the secretion of the hormone melatonin. Yet most of these links are derived from animal studies while the exact functions of the pineal gland in humans are still not well understood.⁽⁴⁾

While the functions of the pineal gland may still be poorly understood, various pathologies of the gland (and region) are well established. Contemporary studies indicate that pineal tumors, whilst rare in adults, comprising about 1% of intracranial tumors, make up to 3-11% of all pediatric intracranial tumors depending upon geographical location and referral patterns in major neurosurgical centers.^(5, 6)

Pineal region tumors can be broadly categorized into germ cell tumors (GCT), tumors arising from the pineal parenchyma and tumors arising from adjacent structures.⁽⁷⁾ These broad categories are further subdivided into multiple tumor types as will be discussed later. The clinical presentation is usually that of mass effect, irrespective of the tumor pathology. One of the most common presentations is hydrocephalus (symptoms of increased intracranial pressure) and may require special attention and a dedicated surgical treatment. Other manifestations include Parinaud syndrome, diplopia, diabetes insipidus, precocious puberty and hemiparesis, among others.⁽⁸⁾

Some GCTs can be identified using certain biomarkers they secrete into the cerebrospinal fluid (CSF) and the blood stream, including alpha fetoprotein (AFP), Beta human chorionic gonadotropin (BHCG) and placental alkaline phosphatase (PLAP).⁽⁹⁾ Otherwise, it is not possible to establish a definitive pathological diagnosis in the absence of positive serum or CSF biomarkers despite the great advances in imaging techniques.⁽⁷⁾

Management decisions regarding adjuvant therapy, prognosis, and follow-up strategies vary with the histologic diagnosis. Hence, a tissue diagnosis is imperative in most cases. Tissue diagnosis could be obtained via biopsy or open resection. Biopsy can be done stereotactically or via endoscopy. The latter can also be used to relieve hydrocephalus by means of an endoscopic third ventriculostomy.⁽¹⁰⁾

Surgical resection is the mainstay treatment in most hemispheric and cerebellar intrinsic tumors. Combined, these comprise the majority of primary brain tumors. Adjuvant treatment is then decided based on the pathology identified from the surgical specimen and even sometimes varies based on the degree of resection.⁽¹¹⁾ This paradigm is different with pineal region tumors where the most common type are GCTs. Many GCTs can be managed by adjuvant treatment alone provided they are properly identified and categorized first.⁽¹²⁾ Moreover, open resection of pineal region tumors is generally more challenging than with the other more common tumors. This is not just due to the former's deep-seated location, but also due to their intimate relationship to important vascular structures.⁽¹⁰⁾

It is then natural that minimally invasive biopsy techniques play a more central role in management of pineal region tumors than with other tumor locations. These techniques include stereotactic and endoscopic modalities. Stereotactic biopsy has the advantage of being able to target virtually any part of the tumor for a better diagnostic yield, while endoscopic biopsies can be combined with ETV for definitive treatment of the frequently associated hydrocephalus. Yet the diagnostic yield and overall safety of either procedure remain the main priority of the treating surgeon.⁽¹³⁾

Our systematic review of the literature will try to answer this important clinical question: among stereotactic and endoscopic biopsy of pineal region tumors, which procedure carries a higher diagnostic yield and a better safety profile.

Aim of the study

The aim of this study is to compare the diagnostic accuracy and the safety profile of endoscopic and stereotactic biopsy of pineal region tumors. The diagnostic accuracy will be reflected through the pathological yield of both biopsy techniques, while the safety profile will be reflected through the differences in morbidity and mortality rates.

This will be done through a systematic review of the literature over the last 30 years.

The Pineal Region⁽¹⁴⁾

The pineal region is an area that is deeply seated in the brain, characterized with its complex anatomy. It's our main topic of interest. It has various structures, where the Pineal gland/body is the star of it, since the whole region with its heterogeneity is named after it. The pineal region is situated in the posterior part of the incisural space. This region includes the pineal body inside the quadrigeminal arachnoid cistern.⁽¹⁵⁾

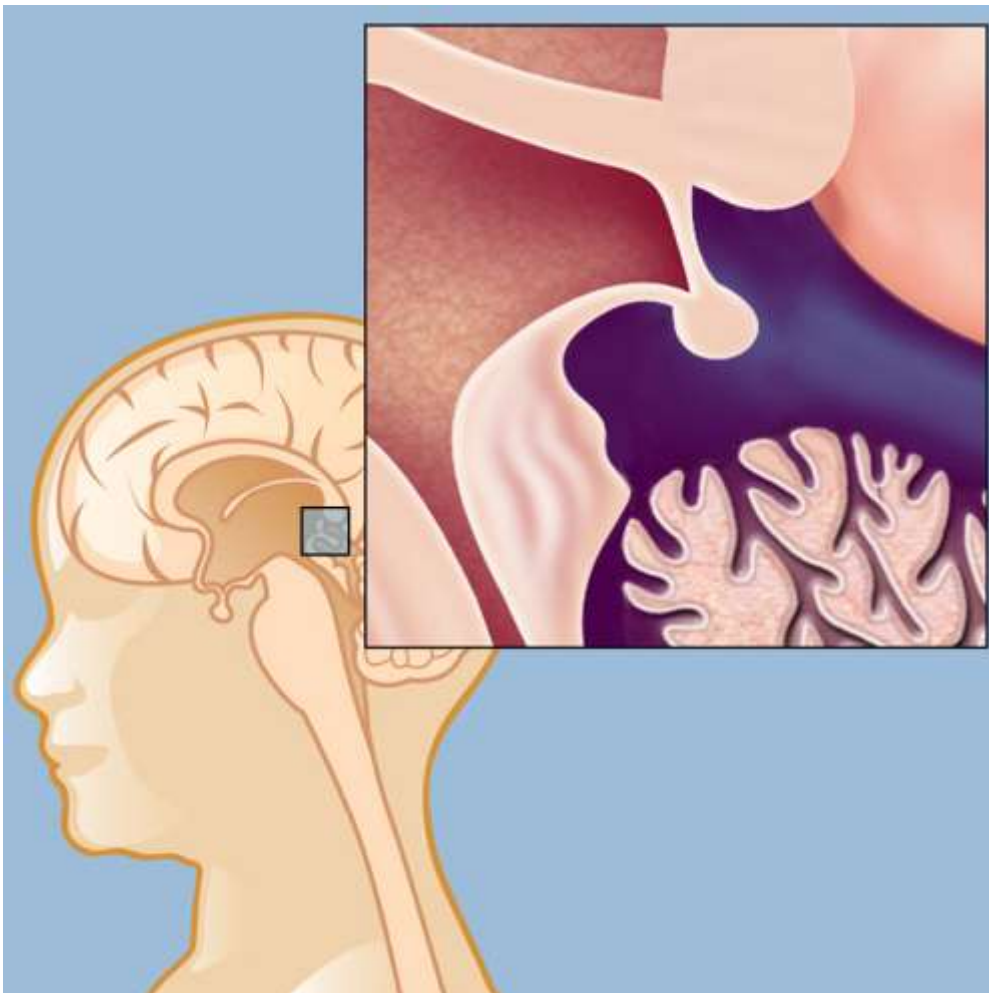


Fig. 1-A. Illustration to where the pineal region is and what it comprises.

Available from:

https://operativeneurosurgery.com/lib/exe/detail.php?id=pineal_region&media=pineal_region.jpg

The Pineal Gland and The Pineal Region

The pineal gland also called epiphysis cerebri, is one of the deep -midline-brain structures found at the center of the skull. It forms an appendix of the caudal end of the diencephalon embracing the pineal recess of third ventricle.

“Pineal” is derived from the Latin word pinealis, meaning pinecone. It has also been referred to as the epiphysis, or “what is grown on something”. Vesalius (1514–1564) elaborately described the topography and consistency of the pineal gland.

Descartes (1596–1650) ⁽¹⁶⁾ believed at this time that it housed the soul. Its deep location made its anatomical description and functional exploration difficult and limited over a long period of time. Until the middle of the 19th century, no significant studies were performed regarding pineal anatomy or function. Then, appears an interest in pineal comparative anatomy, histology, and embryology, owing to the development of more refined sectioning and staining methods. A major breakthrough in pineal studies occurred in the second part of the 20th century with the demonstration of its neuro-humoral functions and its potential role in the regulation of mammalian reproduction and many circadian rhythms ⁽¹⁶⁾. The pineal region includes the pineal body inside the quadrigeminal cistern (Figs. 1 and 2) and the surrounding structures i.e.: posterior third ventricle, tectum, the venous complex, thalami and splenium of corpus callosum (Fig. 3). Meanwhile, the complex anatomic aspect of neurovascular structures and arachnoid membranes in this region has been recently well described in the literature.