Introduction

Until recently, the gold standard for parathyroidectomy was the bilateral neck exploration first described by Mandl in 1926. It was not until the early 1980s that Tibblin and colleagues 1982 first proposed limited neck exploration. Martinez and colleagues then described the use of a handheld probe for intraoperative localization of 99mTc-labeled parathyroid glands in 1995, and Norman and Chheda developed the first Minimally Invasive Radioguided Parathyroidectomy (MIRP) protocol in 1997. MIRP is based on the finding that hyperplastic or adenomatous parathyroid tissue displays a higher percentage of radioactivity than its surrounding tissue after infusion of 99mTc sestamibi **(Michael et al, 2008).**

Brunaud et al 2003 have recently addressed the issue of the definition of ‘‘minimally invasive’’ and describe it as the ability of the surgeon to perform traditional surgical procedures in novel ways that minimize the trauma of surgical exposure, with the principal advantage of a smaller incision, and this include: minimally invasive parathyroidectomy (MIP), focused lateral exploration (FLE), unilateral exploration under local anesthetic (UELA), minimally invasive, videoscopically assisted parathyroidectomy (MIVAP), endoscopically assisted, minimally invasive parathyroidectomy (EAMIP), or minimally invasive, radio-guided parathyroidectomy (MIRP) **(Fausto and Leigh, 2004).**

The benefits of MIRP include reduced operating time, reduced cost, smaller incisions, and fewer complications. With the increase in the availability of microsurgery instruments, gamma probes, rapid parathyroid hormone assays, and endoscopic instrumentation, MIRP has become a reliable method of treating parathyroid disease **(Michael et al, 2008).**

With recent advances that include preoperative parathyroid localization with Sestamibi single photon emission computed tomography (SPECT) or ultrasound (US) with rapid Intraoperative Parathyroid hormone Monitoring (IPM), limited or ‘‘focused’’ parathyroidectomy performed through a small cervical incision serves as an attractive alternative to conventional bilateral cervical exploration (BNE) for primary hyperparathyroidism **(John and Carmen, 2009).**

Combined sestamibi and US can increase accuracy of localization of a single adenoma from 94% to 99%. When concordant, sestamibi and US localization have been reported to have an operative success rate approaching 99%, obviating the need for IPM **(Melanie and David, 2010).**

Intraoperative Parathyroid hormone Monitoring (IPM) can confirm adequate removal of all hyperfunctioning parathyroid glands and predict operative success with reduced operative time compared with BNE. IPM is possible due to the short half-life (3.5–5 minutes) of Parathyroid Hormone (PTH). IPM involves the rapid assay measurement of preoperative, preexcision, and postexcision PTH levels at 5 and 10 minutes after removal of all hypersecreting parathyroid glands **(John and Carmen, 2009).**

Aim of the Work

This work aims at reviewing the literature dealing recent Minimally Invasive Parathyroid Surgery to highlight the recent surgical techniques and methods of accurate preoperative and intraoperative parathyroid localization.

Relevant Anatomy of Parathyroid Gland

Embryology:

The parathyroid bodies arise as a proliferation of endodermal cells at the lateral tip of the third and fourth pharyngeal pouches. The third pouch gives rise to the inferior parathyroid glands and the thymus, which will migrate to the mediastinum. The fourth pouch gives rise to the superior parathyroid glands (fig.1) **(Sanders and Cady, 1991).**

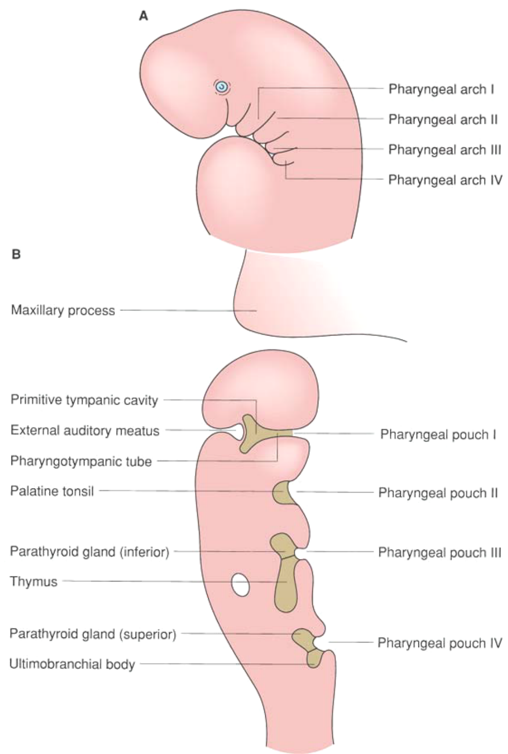

Figure (1): Parathyroid proliferation from pharyngeal pouch ***(Quoted after Doherty, 2006).***

During embryogenesis, the upper and lower parathyroids lay in close proximity to the thyroid and thymus glands, but as fetal maturation progress, separation of adjacent structures occurs (fig.2). Anomalies in the migration of lower parathyroid are more common than the upper glands ***(Cohn and Silen, 1982).***

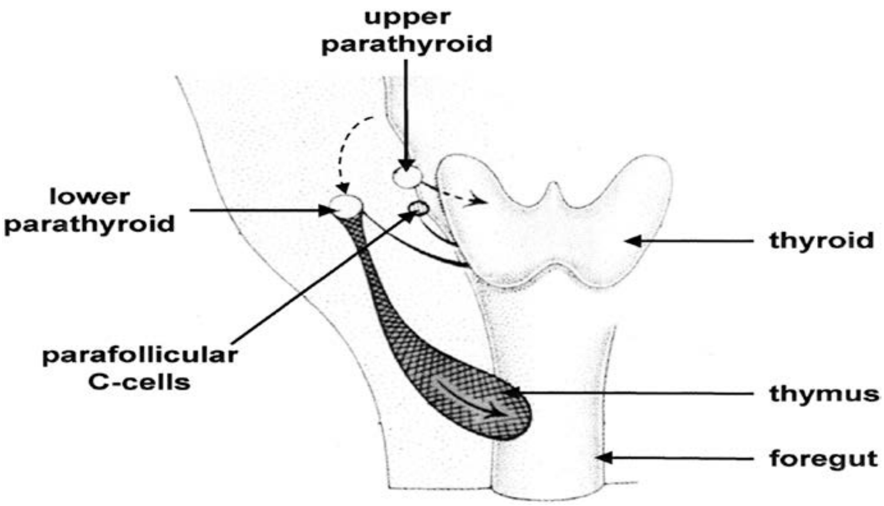

Figure (2): Routes of descent of thymus, parathyroid glands and last branchial body during fetal life **(Quoted after *Cohn and Silen, 1982).***

Normally there are four parathyroid glands in number, two on each side. Each gland measures approximately 6 x 4 x 2 mm and weighs approximately 30–50 mg (total weight, approximately 130–140 mg). Superior and inferior glands are symmetrically arranged and located in relation to posterior surface of the thyroid gland. The superior lies in relation to posterior border of the middle and the upper third of the thyroid. The inferior lies in relation to posterolateral surface of the lower third but the incidence of its abnormal location is high. The anastomotic connection between the superior and inferior thyroid arteries along the posterior thyroid border usually passes very close to the parathyroids (Fig.3). The superior gland is more posterior and medial near the cricothyroid membrane posterior to the point of entry of the recurrent laryngeal nerve and about 1 cm above the entrance of the inferior thyroid artery in the thyroid gland. The inferior gland is usually ventral to the recurrent laryngeal nerve and inferior to the course of the inferior thyroid artery by 1cm close to the lower pole of the thyroid gland ***(Wang, 1977).***

The parathyroid glands are usually separated from the thyroid gland, each with its own capsule of connective tissue. Occasionally they are included in the thyroid capsule that is intracapsular, or even one of them may even follow a blood vessel deep into a sulcus of the thyroid so becomes intraglandular or an intrathyroidal parathyroid gland **(David, 2007)**.

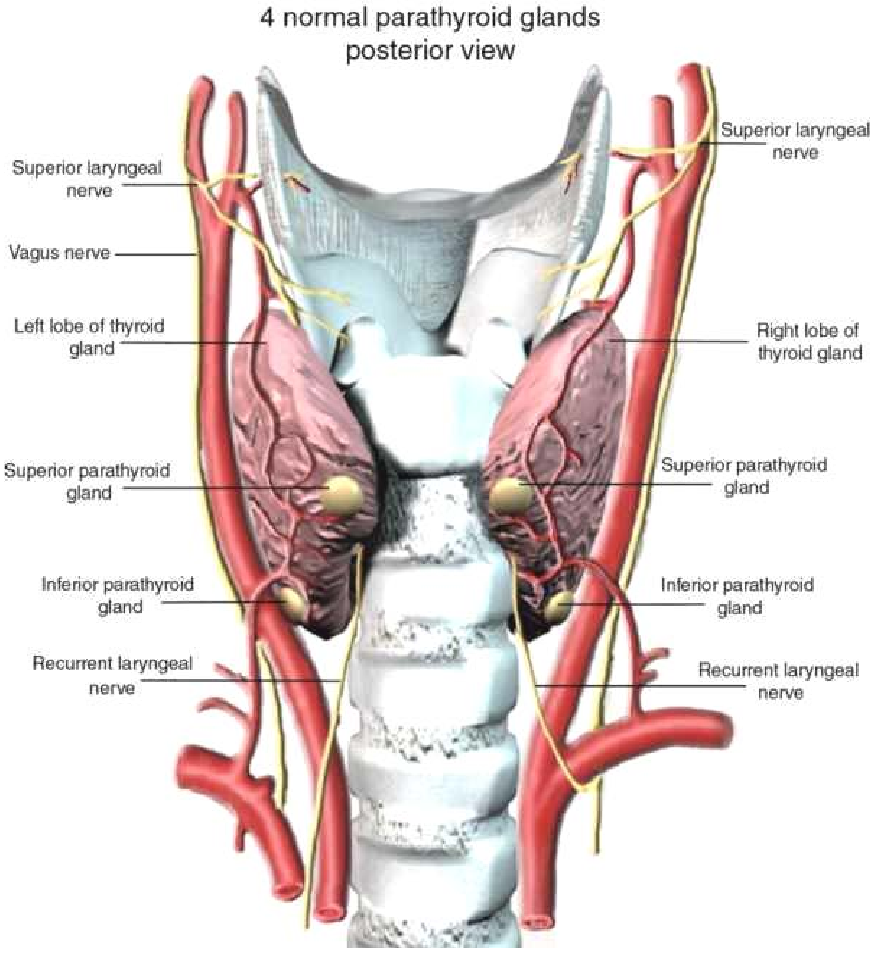

Figure (3): Normally the parathyroid are located on the deep posterior surface of the thyroid gland the superior at the level of the cricoid cartilage, the inferior near to the lower pole and the anastomosis between the inferior and superior thyroid artery runs near to them ***(*****Quoted after** ***Wang, 1977).***

In practice, to localize the gland, the surgeon should start at the point at which the inferior thyroid artery enters the thyroid gland. The superior parathyroid glands will probably lie about one centimeter above it, and the inferior parathyroid glands will probably lie 1.27

cm below it. If the inferior gland is not found, it is more likely to be lower than higher **(Shen et al, 1996).**

Ectopic parathyroid glands occur in 15-20% of patients. Ectopic superior parathyroid glands may be retroesophageal, intrathyroidal, or in the posterior mediastinum. Inferior parathyroid glands have more variable ectopic sites as a result of their longer migration. These sites include the thyrothymic tissue, thyroid, thymus, anterior mediastinum, and within the carotid sheath. Understanding of this anatomic variability is important in interpreting preoperative imaging and directing operative exploration **(Rosen et al, 2012).**

1. Arterial blood supply:

The glands have a rich blood supply from the inferior thyroid arteries or from anastomosis between the superior and inferior vessels. The superior and inferior parathyroids usually supplied by the inferior thyroid artery in 86.1 % on the right side, and in 76.8% on the left. In the absence of an inferior thyroid artery, the superior thyroid artery supplies both the superior and inferior parathyroid glands in the majority of cases. The anastomotic branch between the superior thyroid artery and the inferior thyroid artery supplies the superior parathyroid gland in approximately 45% of cases **(Mariani et al, 2003).**

2. Venous drainage:

The normal venous return of parathyroid gland takes place via the superior, middle, and inferior thyroid veins. The superior and middle thyroid veins in turn drain into the internal jugular veins bilaterally, whereas the inferior thyroid veins normally empty into the left brachiocephalic vein. Ectopic mediastinal and thymic parathyroid tissue usually drains via the thymic or internal thoracic veins **(Chaffanjon et al, 2004*)*.**

3. Lymphatic drainage

Lymph vessels are numerous and associated with those of the thyroid and thymus glands to prelaryngeal, pretracheal, and paratracheal lymph nodes. Laterally, lymph vessels located along the superior thyroid veins pass to the inferior deep cervical lymph nodes. Some lymph vessels may drain into the brachiocephalic lymph nodes or empty directly into the thoracic duct **(Chaffanjon et al, 2004)**.

Histology of Parathyroid Glands

Parathyroid glands consist of chief and oxyphil cells, fibrovascular stroma, and adipose tissue (fig.4). Chief cells are identified in children and adults, while oxyphil cells are mainly observed in adults. Chief cells constitute almost all the parenchyma, their cytoplasm contains argyrophilic granules and lipids. Clear cells have an optically clear cytoplasm as a result of glycogen loss during histologic processing. The total number of oxyphil cells grows with increasing age; however, this kind of cell is also identified in pediatric populations. It is associated with secretory functions, contrary to the usual point of view that these are degenerated cells **(Abujawdeh et al, 1992).**

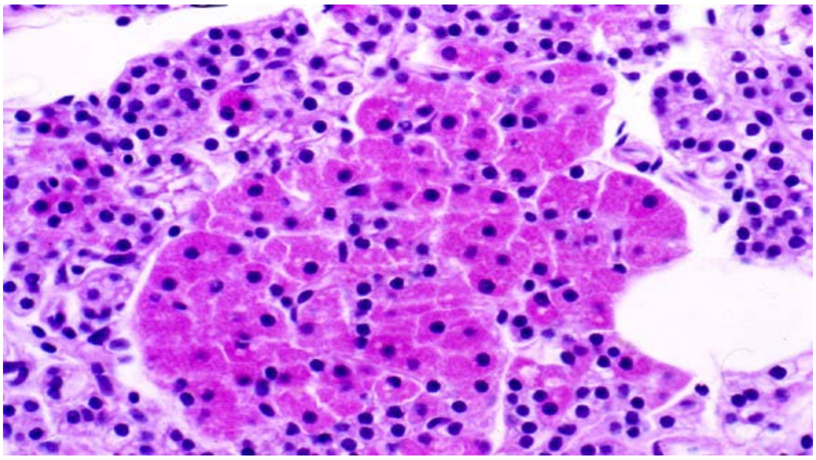

Figure (4): Histology of the normal parathyroid glands **(Abujawdeh et al, 1992).**

Parenchymal cells are arranged in solid sheets, cords, tubular structures, or in 2% to 50%, microcystic formations. The admixture of stromal and adipose elements varies with age and function. The parenchyma-to stroma ratio is used as an indicator of a normocellular or hypercellular gland; the median ratio is 50%, but the adipose tissue content varies from 40% to 70%. Therefore, some authors consider the stromal-parenchymal index inadequate for separating normal from abnormal glands ***(Delellis, 1993*****).**

PHYSIOLOGY OF PARATHYROID GLANDS

The primary physiologic role of the parathyroid gland is the endocrine regulation of calcium and phosphate metabolism. Daily exchanges of these ions from the gastrointestinal tract, bone, and kidney occur (fig.5).

1. Calcium

Calcium ion plays a critical role in all biologic systems. It participates in enzymatic reactions and is a mediator in hormone metabolism. Calcium is intimately involved in the physiology of neurotransmission, muscle contraction, and blood coagulation. It is the major cation in bone and teeth. It represents about 2% of the average body weight, and almost all calcium is contained in the skeleton. The normal range of serum calcium is 9 to 10.5 mg/Dl (4.5 to 5.2 mEq/L). About half of the total serum calcium is in an ionized, biologically active form; 40% is bound to serum protein, mainly albumin, and 10% forms compounds with organic ions, such as citrate. For every change of 1 g/dL in the serum albumin level, a direct alteration of 0.8 mg/dL occurs in the serum calcium concentration **(Doherty, 2006).**

2. Phosphate

Phosphate anion is also an integral component of most biologic systems. It is critical to the pathways of glycolysis and is the functional group for a number of high-energy transfer compounds, including adenosine triphosphate. It is also the major anion in crystalline bone. Normal levels of plasma phosphate range from 2.5 to 4.3 mg/dL, and the level varies inversely with the serum level of calcium **(Doherty, 2006).**

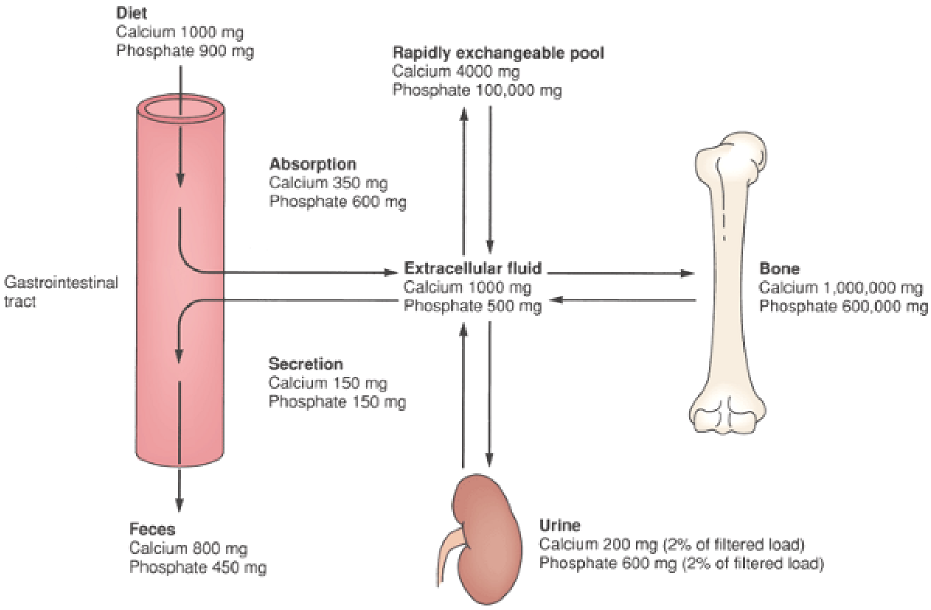

Figure (5): Average daily calcium and phosphate turnover in human **(Quoted after Doherty, 2006).**

Regulation of Calcium and Phosphate Metabolism

The maintenance of calcium and phosphate homeostasis depends on major contributions from three organ systems: The gastrointestinal tract, the skeleton, and the kidneys with minor contributions from the skin and liver. The primary hormonal regulators of this metabolism are parathyroid hormone (PTH), vitamin D, and calcitonin. The actions of each of these hormones in the organs are summarized in Table 1 **(Doherty, 2006).**

Table (1): Hormonal regulation of calcium and phosphate metabolism **(**Doherty, 2006)**.**

Location	PTH	Vitamin D	Calcitonin
GIT	No direct effect	Stimulate calcium and phosphate absorption	No direct effect
Skeleton	Stimulates calcium and phosphate resorption	Stimulates calcium and phosphate resorption	Inhibits calcium and phosphate resorption
Kidneys	Stimulates calcium resorption	No direct effect	Inhibits Calcium and phosphate resorption