

The Effects of Cinacalcet on Parathyroid Adenoma Localization

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INTRODUCTION

Primary Hyperparathyroidism (PHPT)

- Abnormal regulation of parathyroid hormone (PTH) resulting in hypersecretion relative to the serum Ca concentration, most often due to a **solitary benign adenoma (80%)**
- Elevated serum calcium level (1-1.5 mg/dL above the ULN), elevated or inappropriately normal PTH level
- Primarily treated with **parathyroidectomy** (gold standard)
 - Indicated for patients with symptomatic PHPT and asymptomatic patients <50 years of age
 - 3-4:1 F:M, increased incidence in Black individuals

Cinacalcet (Sensipar)

- Positive allosteric modulator of the calcium sensing receptor (CaSR) on parathyroid glands (negative feedback)
- Indicated in some patients with severe hypercalcemia and/or contraindication to parathyroidectomy
- Normalization of Ca²⁺ levels (90% patients); increase in phosphate levels; lack of normalization of PTH levels

Preoperative Imaging Modalities – range of cost, availability, and sensitivity

- Neck ultrasonography (US) [Sensitivity 55-87%] - ↓ Cost, operator dependent
- 99mTc-sestamibi scintigraphy (MIBI) [Sensitivity 70%] - planar images after injection of the radiotracer 99mTc (retained by oxyphil cells in parathyroid glands)
- Sestamibi-single photon emission CT (SPECT) [Sensitivity 74%] - 3D Sestamibi scan, higher resolution. SPECT/CT ==> sensitivity 86%.
- Parathyroid 4D-CT [Sensitivity 92.5%] - Higher resolution, higher cost. Location + movement of tumor

HYPOTHESIS:

CINACALCET REDUCES PREOPERATIVE LOCALIZATION RATES IN PATIENTS WITH PHPT

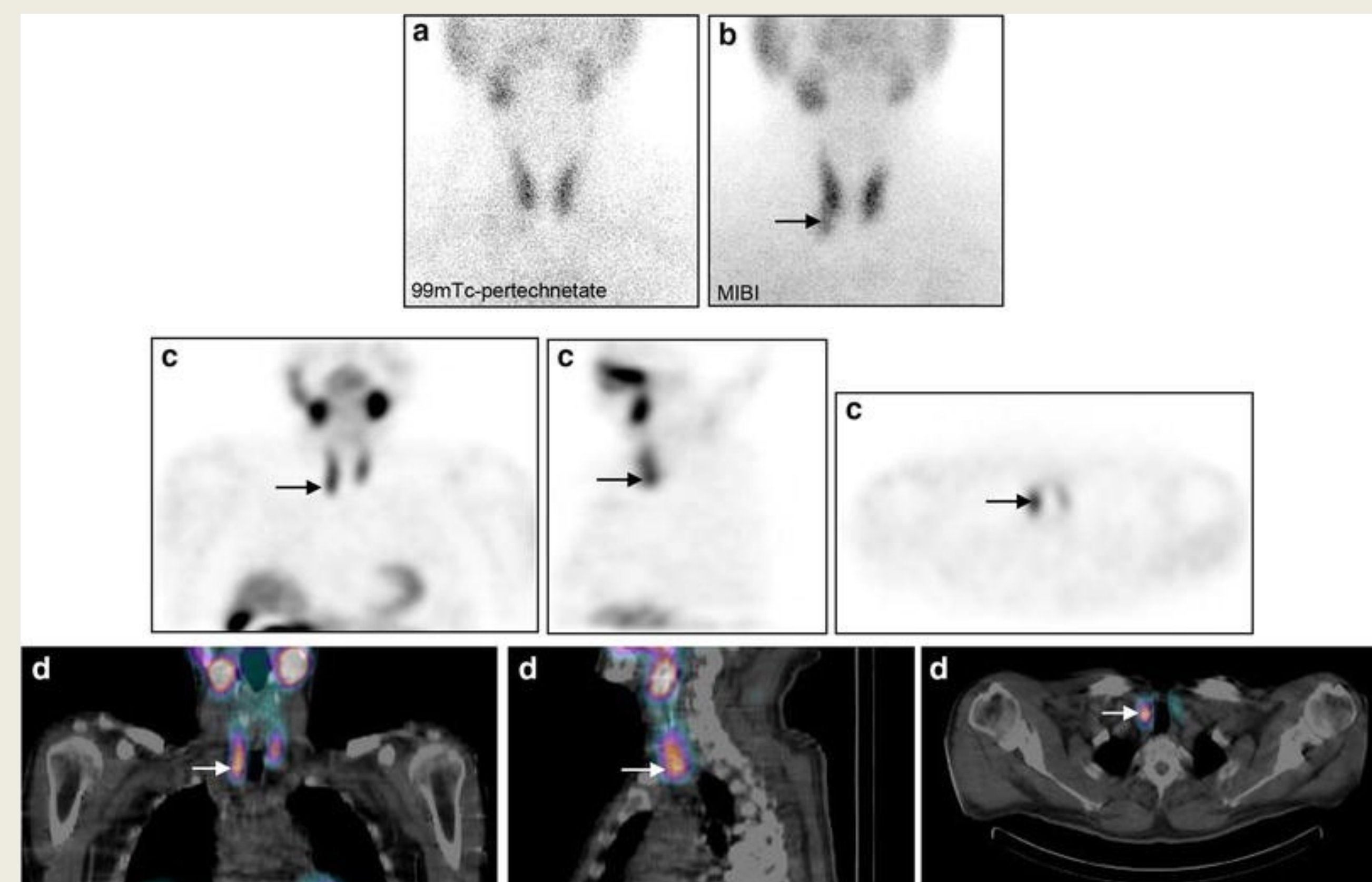


Figure 1. SPECT/CT in Primary Hyperparathyroidism
<https://link.springer.com/article/10.1007/s40336-014-0089-4/figures/2>

METHODS AND MATERIALS

- Retrospective chart review was performed at Memphis VA Medical Center. All patients from 2013 to 2022 who underwent Sestamibi imaging to evaluate PHPT were included. Preoperative and postoperative lab values, imaging findings, operative findings and basic demographic data were collected. Patients were divided into Cinacalcet vs non-Cinacalcet groups and previously mentioned data points, particularly localizing versus non-localizing Sestamibi scans were directly compared.
- VAMC Memphis IRB approval
- Multidisciplinary collaboration [Surgeons, Endocrinology, Radiology]
- Retrospective chart review, repository
 - All patients 2013-2023, undergoing Sestamibi imaging/SPECT CT to evaluate pHPT
 - Cinacalcet vs Non-Cinacalcet groups, analyzed preoperative localization across surgical patients within our cohort
- Operative reports, clinic notes, medications, imaging, pathology
- Fisher exact test (P <0.05)

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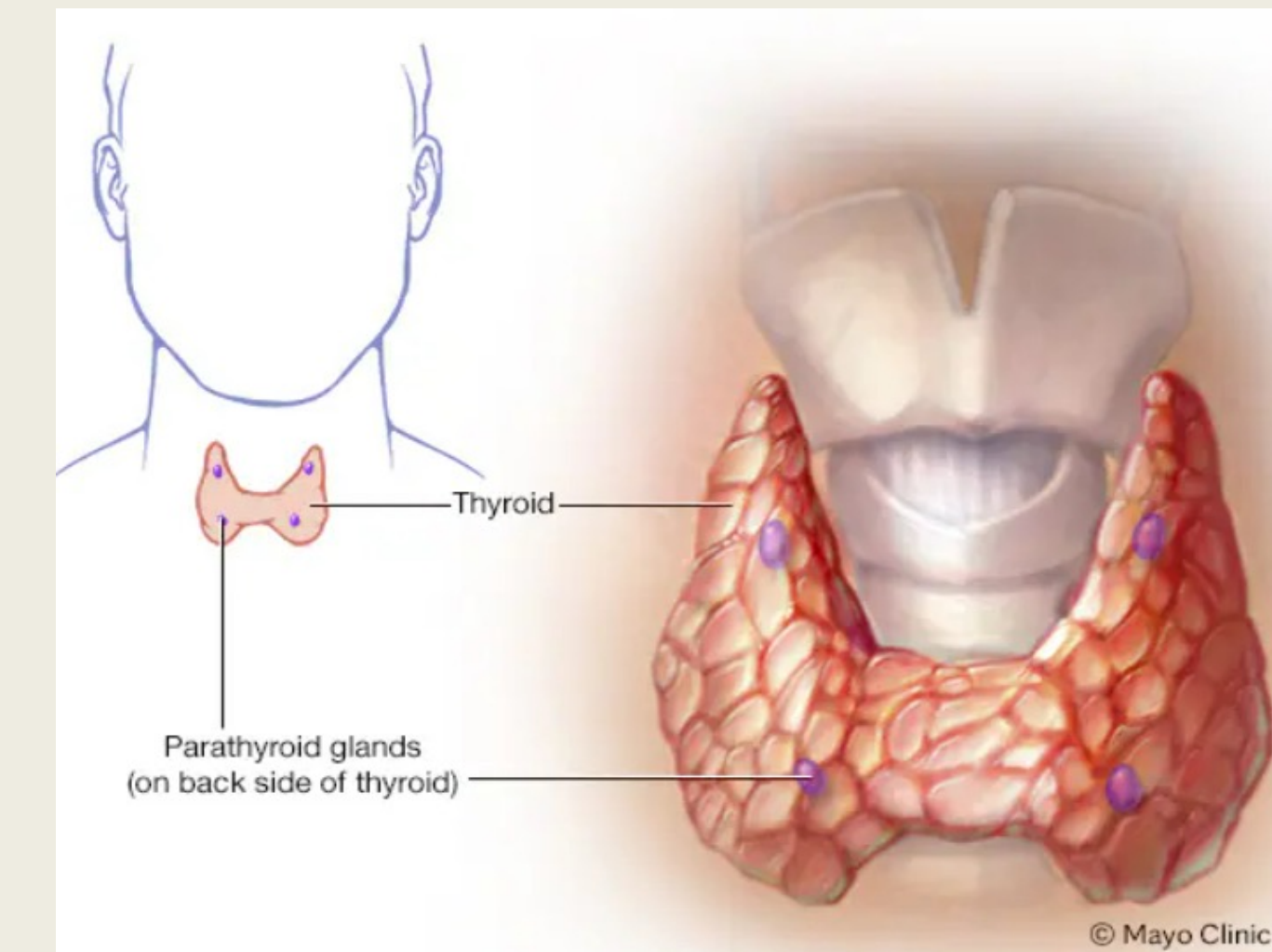


Figure 2. Parathyroid glands (Mayo Clinic)

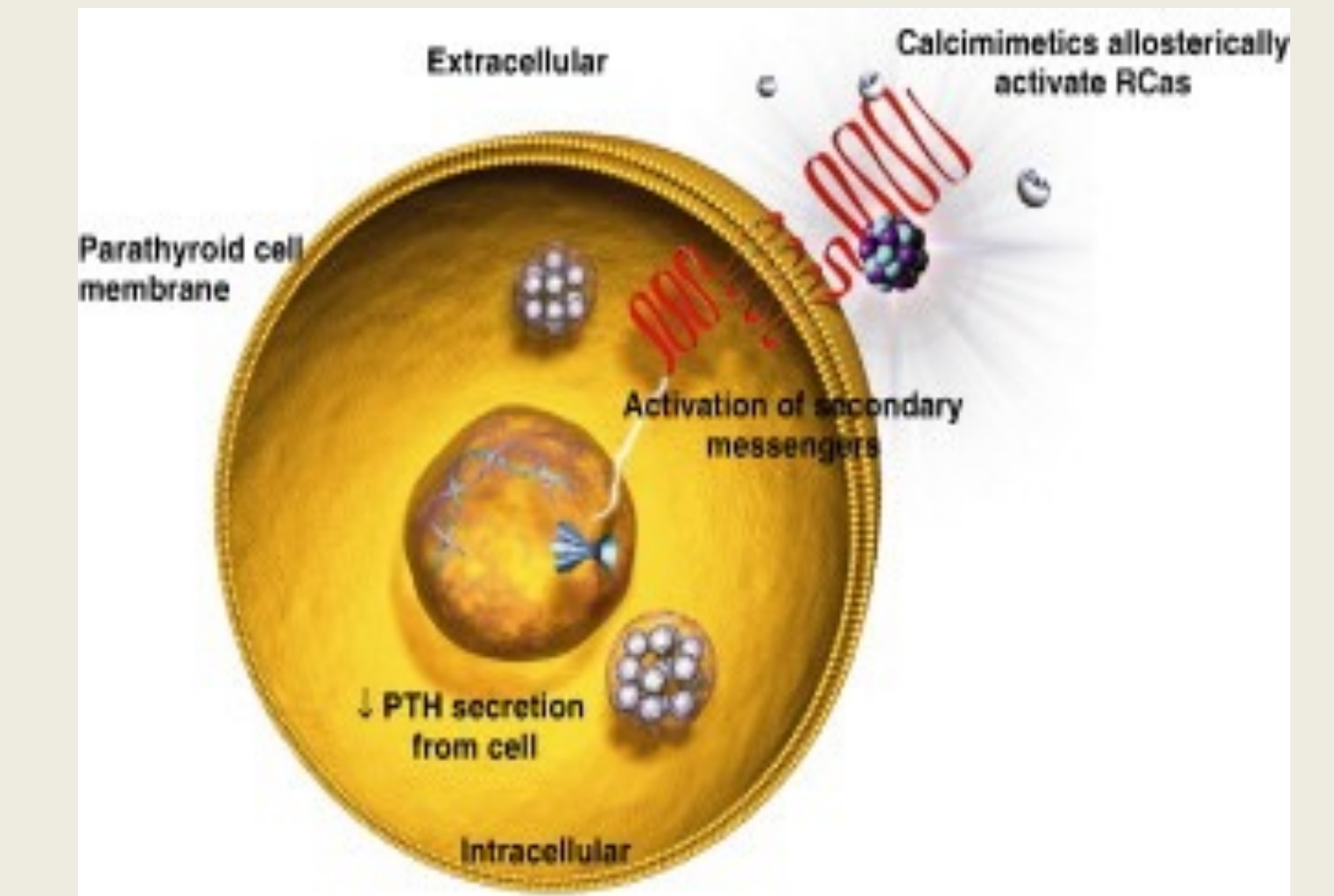


Figure 3. Cinacalcet - Mechanism of Action.

RESULTS

159 patients – ENT/General surgery [48 surgical, 111 nonsurgical]
-- Primarily male [Male 77%, Female 23%; Avg. Age 67]

-- Nonsurgical cohort: [Cinacalcet] – 49 (44% -- 49/111); [Non-Cinacalcet Group] – 62 (56% -- 62/111)

Cinacalcet cohort

- Surgical patients – 25 (52% – 25/48 on Cinacalcet; **56% localizing**)

Non-Cinacalcet cohort

- Surgical patients – 23 (48% – 23/48 on Cinacalcet; **87% localizing**)

Results			
	Cinacalcet	Non-Cinacalcet	Marginal Row Totals
Localizing	14	20	34
Non-Localizing	11	3	14
Marginal Column Totals	25	23	48 (Grand Total)

The Fisher exact test statistic value is 0.0267. The result is significant at p < .05.

DISCUSSION

Practice patterns – Availability/Endocrinology

Broad/liberal use of Cinacalcet, cost
Endocrine conference, collaborative approach and preoperative planning
Previous studies (reduction in size, decreased uptake, apoptosis)

Implications:

Patients who have been treated with Cinacalcet are significantly more likely to have non-localizing preoperative Sestamibi-SPECT/CT scans (56% vs. 87%), p < 0.0267

Limitations:

- Single institution, VA population (older, male predominance, comorbidities, atypical practice patterns, surgical aversions),
- Large # of nonsurgical patients in our cohort

Retrospective chart review [Reports/CPRS, medication list]

-[Exact time-frame of use, compliance to medication, timing of imaging]

Consistency/reproducibility, Variable regional quality

FUTURE STUDY

- The role of Cinacalcet and optimization of preoperative imaging modalities
- Multi-institutional study, replication across populations – Broader utilization of VA repository
- Effects of comorbidities, cotreatments on pharmacokinetics
- Integrated comparison of calcium, vitamin D, and additional laboratory values over time

CONCLUSIONS

Patients who are currently taking or have previously been on Cinacalcet therapy are more likely to have non-localizing Sestamibi scans. Previous studies have suggested reduction in parathyroid adenoma size as well as decreased scintigraphy uptake of adenomas in patients with PHPT for patients on Cinacalcet therapy. Further research is required to determine if these patients would benefit from optimization of timing and modality of first line imaging for preoperative planning.