Supplemental Material

Supplementary Table 1. Total costs and quality-adjusted life years (QALYs) for the non-dominated interventions of the base case analysis with variable discount rates

Intervention	Discount rate	Total costs [$]	Total QALYs	Incremental costs [$]	Incremental QALYs	ICER [$/QALY]	INMB
4D-CT without ioPTH	3%	10,276	15.333	-	-	-	-
FCH-PET/CT without ioPTH	3%	11,619	15.352	1343	0.018	73,251	416
4D-CT without ioPTH	1.5%	10,276	17.805	-	-	-	-
FCH-PET/CT without ioPTH	1.5%	11,619	17.827	1343	0.021	63,082	700
4D-CT without ioPTH	0%	10,289	20.889	-	-	-	-
FCH-PET/CT without ioPTH	0%	11,623	20.914	1334	0.024	53,414	1062

Abbreviations: ICER, incremental cost-effectiveness ratio; INMB, incremental net monetary benefits.

Supplementary Table 2. Confidence intervals of the Monte-Carlo-Simulation

Intervention	Total costs [$]	QALYs	95 CIs costs [$]	95 CIs QALYs
4D-CT without ioPTH	10282	15.3333	(10286, 10296)	(15.3331, 15.3335)
Ultrasound without ioPTH	10756	15.2971	(10767, 10778)	(15.2969, 15.2973)
4D-CT with ioPTH (Miami criterion)	10772	15.3320	(10777, 10787)	(15.3319, 15.3322)
SPECT/CT without ioPTH	10800	15.3219	(9897, 11108)	(15.3152, 15.3286)
4D-CT with ioPTH (Vienna criterion)	10953	15.3209	(10948, 10958)	(15.3208, 15.3211)
Ultrasound With ioPTH (Miami criterion)	11260	15.2965	(11271, 11282)	(15.2963, 15.2967)
SPECT/CT with ioPTH (Miami criterion)	11349	15.3176	(11108, 11441)	(15.3158, 15.3194)
Ultrasound with ioPTH (Vienna criterion)	11393	15.2890	(11387, 11398)	(15.2888, 15.2892)
SPECT/CT with ioPTH (Vienna criterion)	11507	15.3070	(11471, 11542)	(15.3066, 15.3074)
FCH-PET/CT without ioPTH	11609	15.3520	(11607, 11626)	(15.3519, 15.3521)
FCH-PET/CT with ioPTH (Miami criterion)	12180	15.3492	(12188, 12197)	(15.3491, 15.3494)
FCH-PET/CT with ioPTH (Vienna criterion)	12422	15.3357	(12418, 12426)	(15.3356, 15.3358)

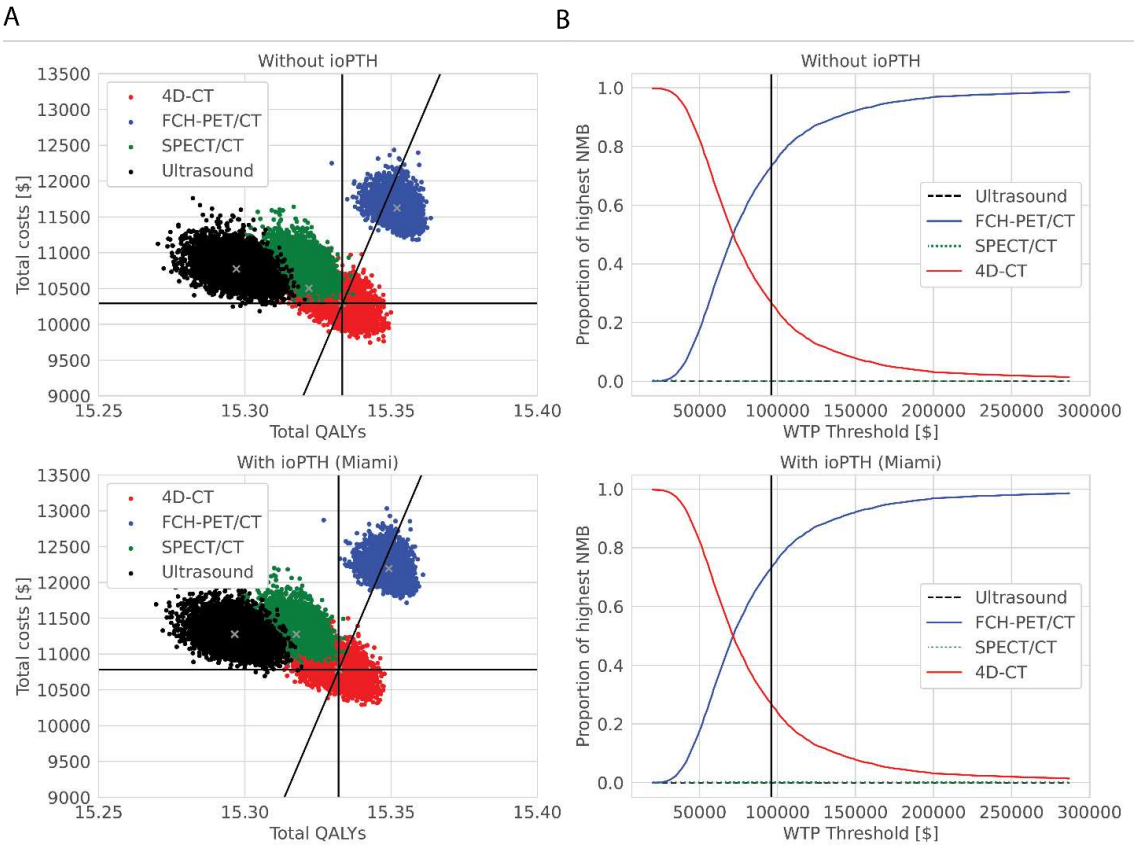
Abbreviations: CI, confidence interval; FCH-PET/CT, ^{18}F-fluorocholine positron emission tomography; ioPTH, intraoperative parathyroid hormone; QALYs, quality-adjusted life years; SPECT/CT, ^{99m}Tc-Sestamibi single-photon-emission computed tomography/computed tomography; 4D-CT, four-dimensional-CT.

Supplementary Table 3. Number of clinical events per 1000 patients for all interventions

Intervention	BNE	Reoperations	Persistent hypopara-thyroidism	Persistent RLN injury	Persistent hypoparathyroidism and RLN injury
4D-CT without ioPTH monitoring	257.45	10.50	2.91	1.68	0.02
4D-CT with ioPTH monitoring (Miami criterion)	274.34	2.77	3.03	1.45	0.02
4D-CT with ioPTH monitoring (Vienna criterion)	347.45	0.58	3.81	1.74	0.02
FCH-PET/CT without ioPTH monitoring	239.68	3.00	2.62	1.30	0.05
FCH-PET/CT with ioPTH monitoring (Miami criterion)	257.29	0.78	2.82	1.30	0.02
FCH-PET/CT with ioPTH monitoring (Vienna criterion)	333.98	0.17	3.66	1.66	0.02
SPECT/CT without ioPTH monitoring	284.55	6.00	3.10	1.64	0.08
SPECT/CT with ioPTH monitoring (Miami criterion)	300.84	1.56	3.29	1.55	0.03
SPECT/CT with ioPTH monitoring (Vienna criterion)	371.52	0.33	4.07	1.85	0.02
Ultrasound without ioPTH monitoring	371.14	3.00	4.06	1.95	0.05
Ultrasound with ioPTH monitoring (Miami criterion)	385.59	0.79	4.22	1.94	0.03
Ultrasound with ioPTH monitoring (Vienna criterion)	448.31	0.16	4.91	2.22	0.03

Abbreviations: BNE, bilateral neck exploration; FCH-PET/CT, ^{18}F-fluorocholine positron emission tomography; ioPTH, intraoperative parathyroid hormone; RLN, recurrent laryngeal nerve; SPECT/CT,^{99m}Tc-Sestamibi single-photon-emission computed tomography/computed tomography; 4D-CT, four-dimensional-CT.

Abbreviation: RLN, recurrent laryngeal nerve.

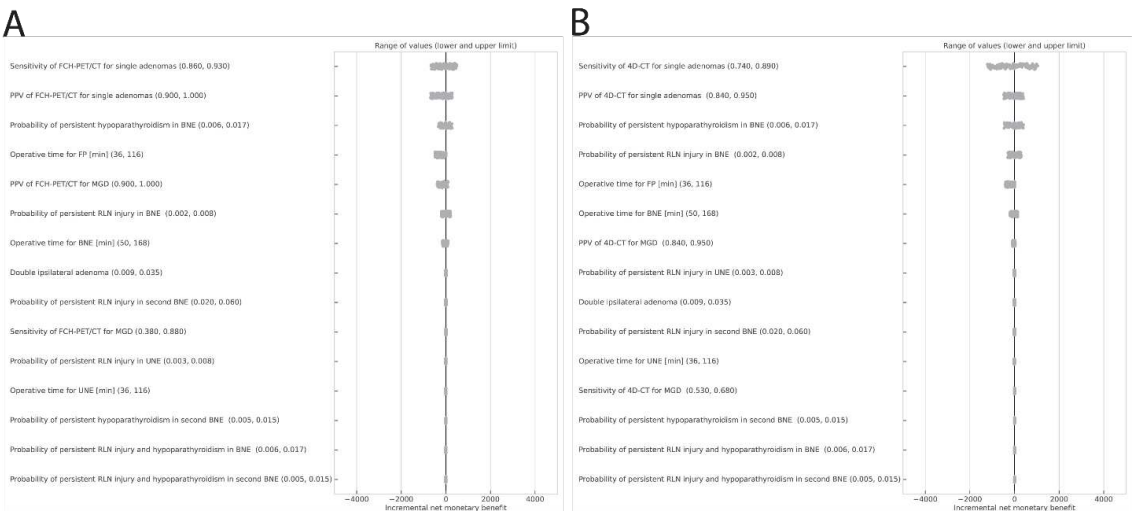


Supplementary Figure 1. Uncertainty analysis.

A: Scatter plots showing the outcomes of the Monte-Carlo-Simulation. The top panel depicts the results of the simulations without ioPTH monitoring, and the bottom panel shows the results of the simulations with ioPTH monitoring using the Miami protocol. For each parameter, beta or gamma distributions were fitted. In all, 5,000 samples were drawn from the distributions and were used for the subsequent analysis in the decision-tree model. Total costs and quality-adjusted life years (QALYs) were calculated for each sample. The mean value of the simulations for each modality is shown as a gray x, and the cost-effectiveness threshold (WTP: $95,958) is depicted as a black line, which was calculated against the least expensive strategy (4D-CT without ioPTH monitoring). The costs and utilities of the least expensive strategy are shown with a black horizontal and vertical line on both plots, respectively.

B: A cost-effectiveness acceptability curve was generated from the result of the Monte Carlo simulation. The top panel depicts the results without the ioPTH monitoring, whereas the bottom

panel shows the results using the Miami protocol for the ioPTH monitoring. We varied the willingness-to-pay (WTP) threshold from 20,000 to three times the WTP of $95,958 ($287,874); and calculated the proportion of the highest net monetary benefit (NMB) for each intervention. Below a WTP threshold of $75,000, 4D-CT without intraoperative parathyroid hormone (ioPTH) monitoring yields the biggest proportion of highest NMBs. Above a WTP threshold of $80,000, ^{18}F-fluorocholine positron emission tomography (FCH-PET/CT) becomes the dominant strategy. In the range of a WTP threshold between $20,000 and $287,874, ^{99m}Tc-Sestamibi single-photon-emission computed tomography [SPECT]/computed tomography [CT] and ultrasound are dominated strategies both without and with ioPTH monitoring. The black vertical line on the panels depicts the US WTP of $95,958.

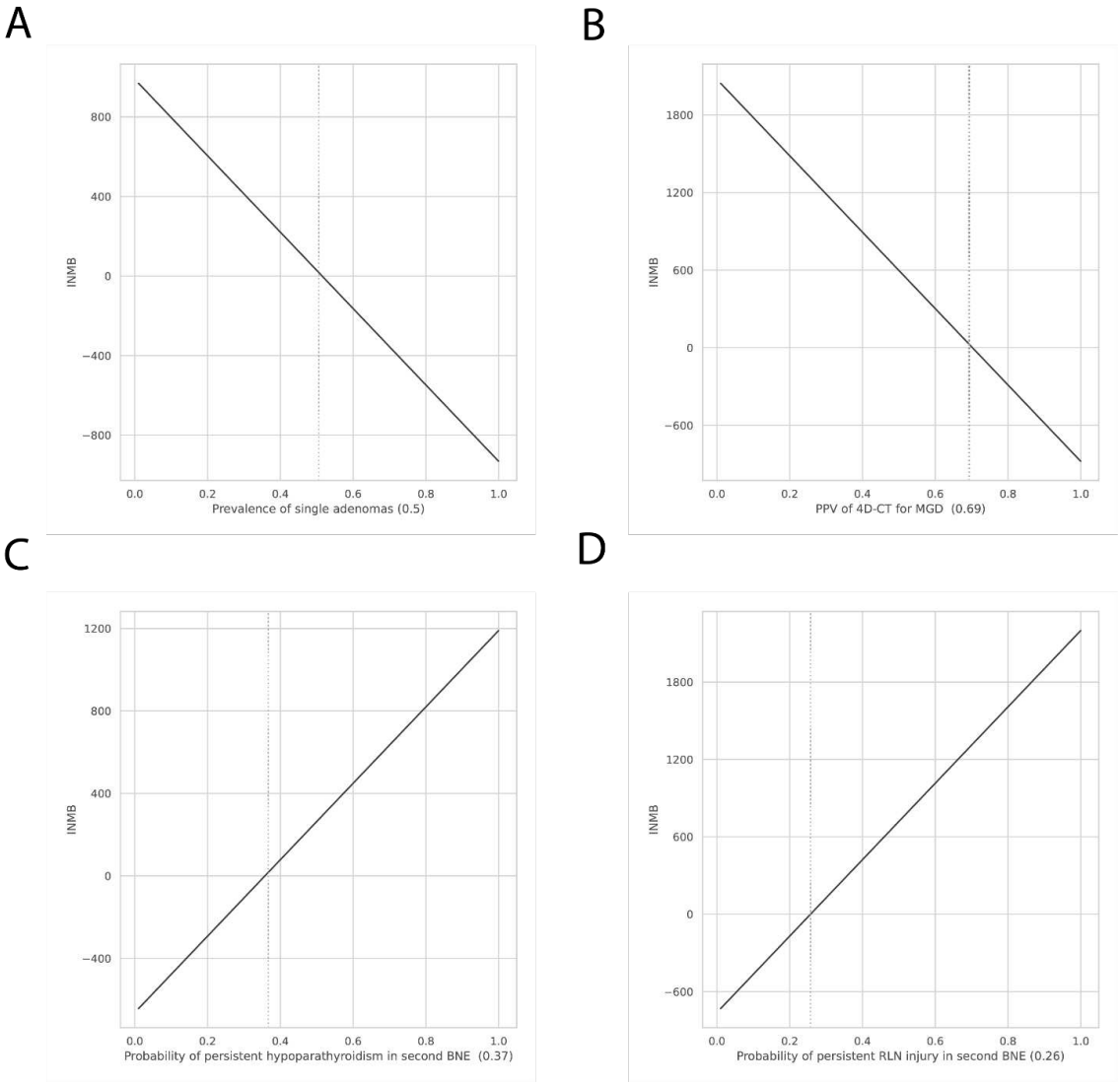


Supplementary Figure 2: One-way sensitivity analysis using the uncertainty estimates of the probabilistic sensitivity analysis

A: Variation of the parameters of the ^{18}F-fluorocholine positron emission tomography (FCH-PET/CT) without intraoperative parathyroid hormone (ioPTH) monitoring using the 95% CIs and ranges applied in the Monte-Carlo-Simulation. Incremental net monetary benefits were calculated in comparison with the base case values of the four-dimensional-computed tomography (4D-CT) without ioPTH monitoring, as this was the least expensive intervention in our base case analysis.

B: Varying the parameters were done in a similar manner as in panel A. Incremental net monetary benefits of 4D-CT with ioPTH monitoring (Miami protocol) were calculated in comparison with the base case values of the 4D-CT without ioPTH monitoring.

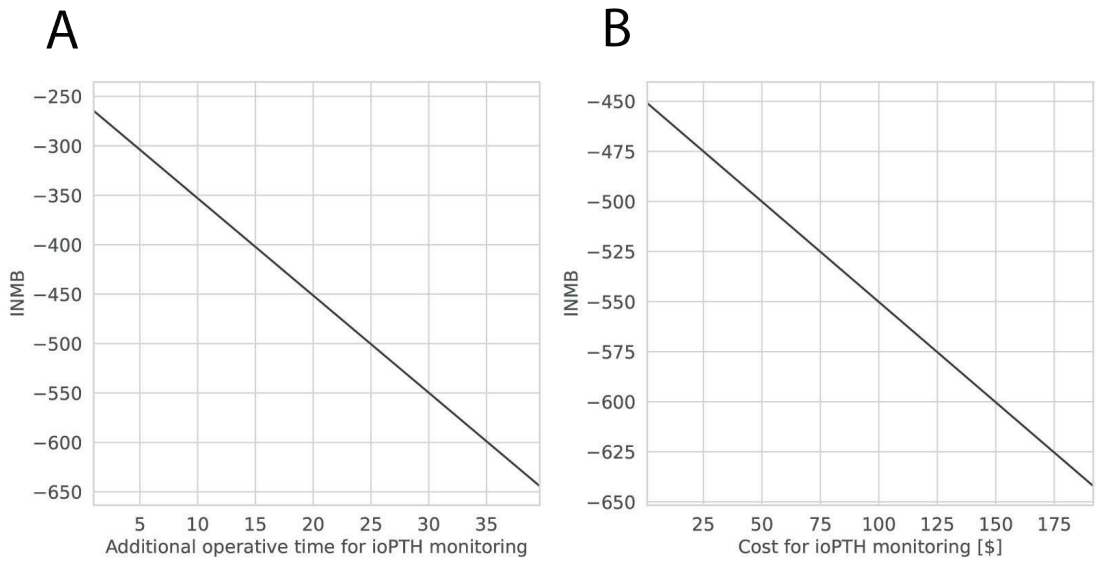
Abbreviations: BNE, bilateral neck exploration; FP, focused parathyroidectomy; MGD, multiglandular disease; PPV, positive predictive value; RLN, recurrent laryngeal nerve; UNE, unilateral neck exploration.



Supplementary Figure 3. Threshold analysis on parameters for the four-dimensional-CT (4D-CT).

Assessment of the theoretical possibility of intraoperative parathyroid hormone (ioPTH) monitoring with a positive net monetary benefit value. Each parameter of the 4D-CT with ioPTH monitoring (Miami criterion) was varied from 0 to 1 for probabilities and utility weights, respectively, and 0 to the base case value for costs. Incremental net monetary benefit (INMB) was calculated in comparison with the 4D-CT without ioPTH monitoring.

Abbreviations: BNE, bilateral neck exploration; INMB, Incremental Net Monetary Benefits; MGD, multiglandular disease; PPV, positive predictive value; RLN, recurrent laryngeal nerve; 4D-CT, four-dimensional-CT.



Supplementary Figure 4. Threshold analysis on the additional time and assay cost for ioPTH monitoring for the four-dimensional-CT (4D-CT).

We varied the additional operative time (A) and the assay cost (B) for ioPTH monitoring (Miami criterion) from its base case value to the theoretical minimum to investigate their impact on the cost-effectiveness of the assay.

Abbreviations: INMB, Incremental Net Monetary Benefits; ioPTH, intraoperative parathyroid hormone monitoring.