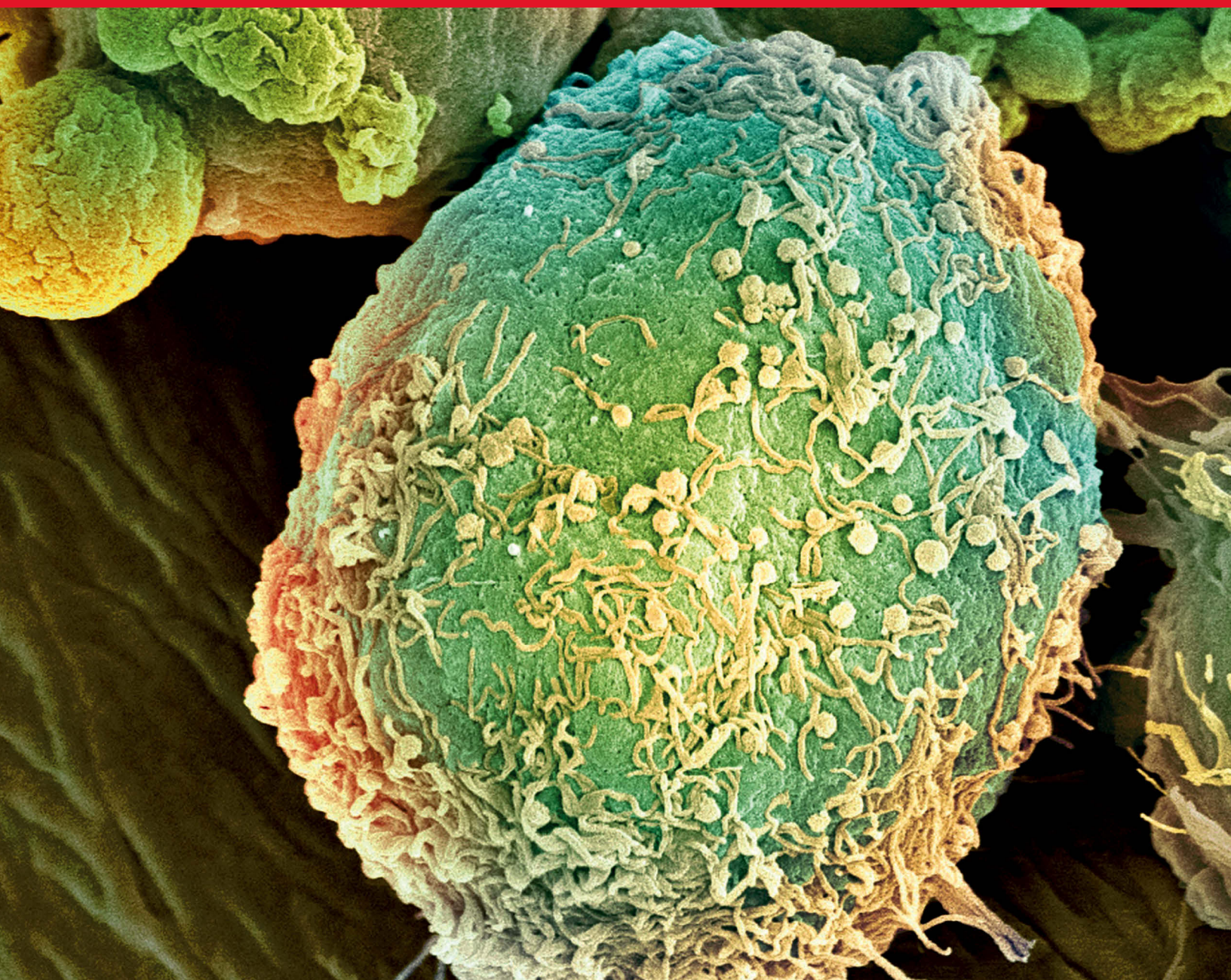


thermoscientific



Fast, Precise, Efficient Monitoring of Neuroendocrine Tumors

B·R·A·H·M·S Chromogranin A and Neuron-Specific
Enolase Immunodiagnostic Assays

ThermoFisher
SCIENTIFIC

Chromogranin A (CgA) – Marker for neuroendocrine tumors

Function of CgA as prohormone

The chromogranins comprise an entire family of glycoproteins, of which Chromogranin A (CgA) and Chromogranin B (CgB) are the best-known representatives. CgA has a molecular weight of 49 kDA and is produced in high concentrations in endocrine and neuroendocrine cells, e.g. in the pancreas, stomach and intestines.³

Its biological function has not yet been determined conclusively, but it is believed that CgA is a prohormone. The precursor molecule of CgA is made up of several peptides such as chromo-statin, pancreastatin and catestatin, which appear individually once the prohormone has been proteolytically processed by various proteases.⁴

CgA and its proteolytic fragments are secreted from the tissue into the blood. Therefore CgA is increasingly important as a marker for endocrine cells and neuroendocrine tumors.⁴

Clinical utility of CgA in neuroendocrine tumors (NETs)

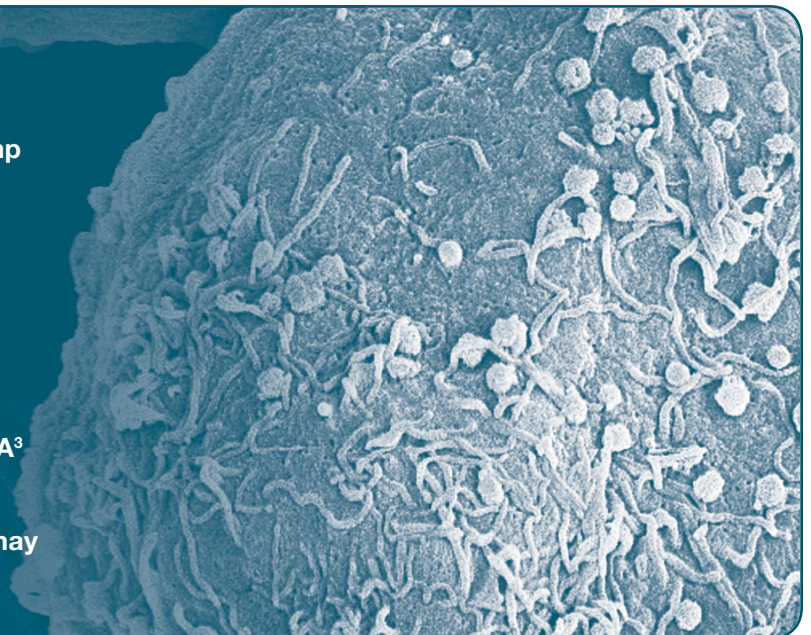
CgA elevations occur in diverse NETs but are usually more pronounced in GEP-NETs (small intestinal, gastric, and pancreatic NETs; GEP = Gastroenteropancreatic). CgA elevations may occur in carcinomas with a complete or a partial neuroendocrine phenotype (Figure 1).³

CgA's particular strengths as a serum tumor marker include:⁴

- **It is already part of the established diagnostic and monitoring procedure for neuroendocrine tumors**
- **It can be used to track further progress of the tumor disease**
- **It presents the option of evaluating the success of a treatment**

When using CgA, consider:

- **Patients who are being treated with proton pump inhibitors (e.g. gastritis) may have an elevated CgA^{1,6,7}**
- **Renal failure may increase detectable CgA by reducing glomerular filtration of CgA-related peptides^{1,6,7}**
- **Patients with chronic/acute inflammation and cardiac insufficiency may have an elevated CgA³**
- **Patients with non malignant gastro intestinal disorders (e.g. pancreatitis, chronic hepatitis) may have an elevated CgA³**



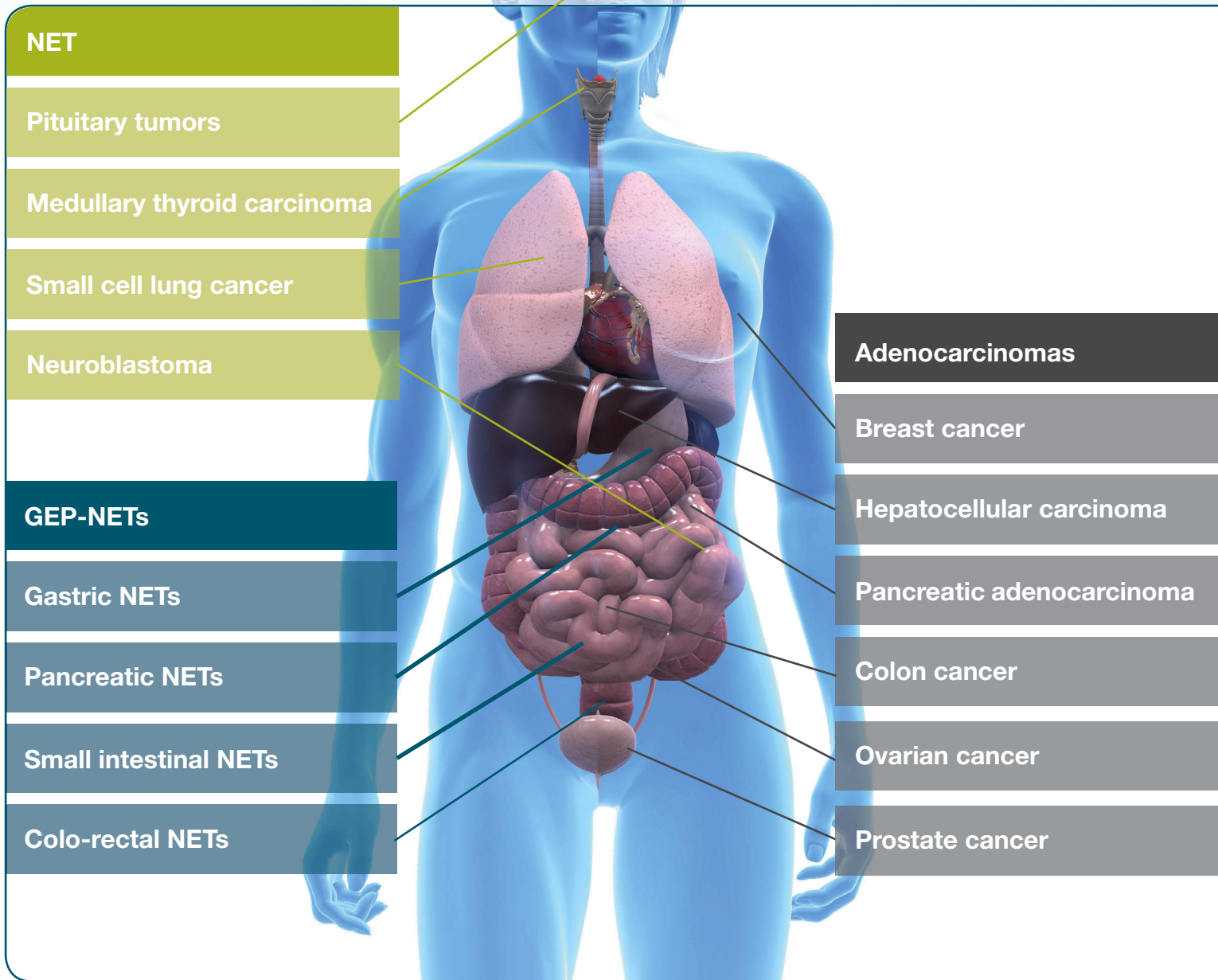


Figure 1: Neoplastic causes of elevated CgA (adapted from Lawrence et al.⁹)

First and only fully automated CgA assay

Shortest time to result

The automated Thermo Scientific™ B·R·A·H·M·S™ KRYPTOR™, a random access analyzer, provides fast, reproducible results and is significantly less labor intensive than other commercially available CgA assays.²

When assessing response to therapy and disease burden clinicians expect results in a timely manner. Results on KRYPTOR are **available within 29 minutes** (Figure 2) and could be reported to clinicians the same day. Labs can now provide to clinicians a reliable monitoring indicator for response to targeted therapy of neuroendocrine tumors.²

Superior precision

KRYPTOR provides exceptional intraand interassay precision due to homogeneous assay design without any washing or separation step.

The extraordinary assay precision supports confident decision making on the patient's clinical status and further therapy for optimal patient management.

Thermo Scientific B·R·A·H·M·S KRYPTOR compact PLUS

Short incubation time (29 min)
enables reliable monitoring

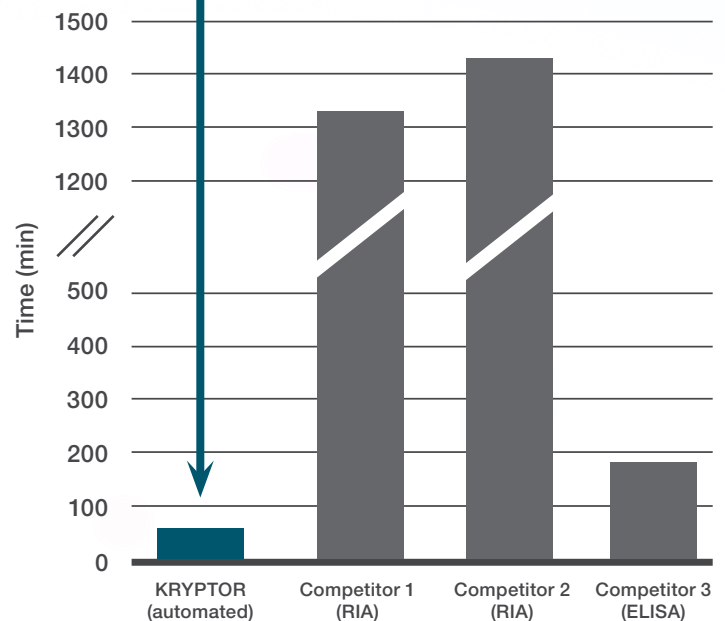
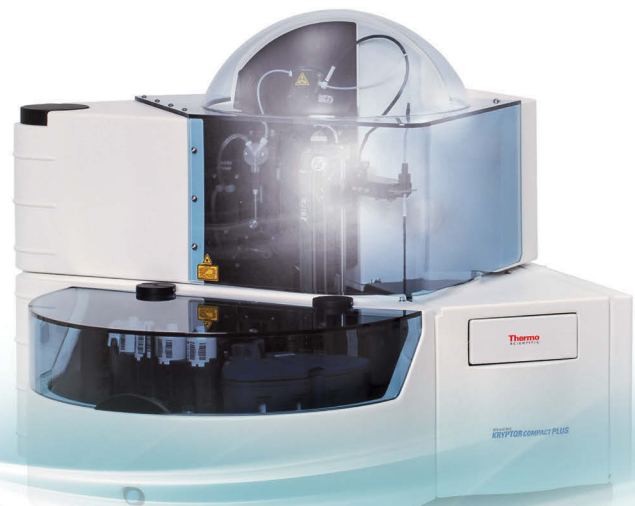


Figure 2: Incubation time (min) of various CgA assays



Broadest measuring range

Each dilution requires an extra determination. On KRYPTOR less samples have to be diluted compared to other current commercially available assays because of the broader direct measuring range (Figure 3).

The Thermo Scientific B·R·A·H·M·S CgA II KRYPTOR assay therefore meets the challenge to provide reliable results over a wide range, **vastly improving the assessment of patients receiving treatment regimes for neuroendocrine tumors.**²

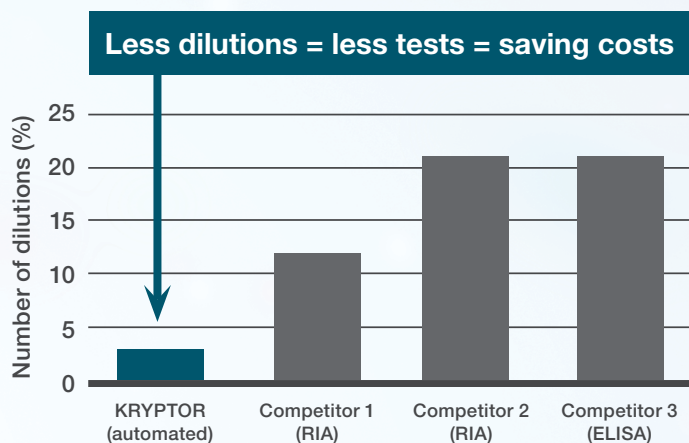


Figure 2: Incubation time (min) of various CgA assays

“The patient group that has been most positively affected by the Chromogranin A assay on KRYPTOR are the **patients with extensive neuroendocrine or carcinoid tumors**. In this group CgA is often extraordinarily high and samples have to be diluted. Accurately quantifying CgA in these patients allows for **improved assessment of disease activity and response to therapy.**”

CgA expert user

Neuron-Specific Enolase (NSE) – Marker in poorly differentiated NETs

Excellent precision for confident cancer monitoring

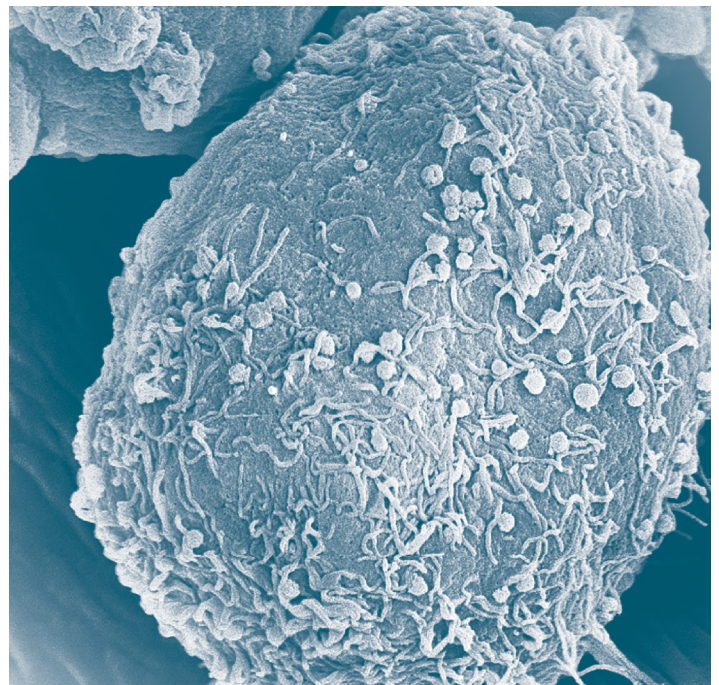
NSE is formed in the neuroendocrine cells of various tissues and subsequently secreted into the blood. NSE is widely used as a marker of neuroendocrine differentiation. It is a cytosolic protein, whose presence does not correlate with granular density. For this reason it is particularly useful for the diagnosis of poorly granulated neoplasm, i.e. poorly differentiated neuroendocrine carcinomas.⁵

However, its expression is not exclusively restricted to neuroendocrine tissue, NSE is also frequently increased in patients with e.g.

- Small cell lung cancer (SCLC)
- Medullary thyroid cancer
- Pheochromocytoma

Increased values for NSE often indicate an increased tumor burden, but it does not correlate with the size of the tumor.

The combination of NSE and CgA results in higher specificity than with the two parameters individually.



Neuroendocrine tumor markers on KRYPTOR Systems

Thermo Scientific B·R·A·H·M·S CgA II KRYPTOR

Article number: 839.050

Assay characteristics

Determinations	50
Sample volume	14 µL
Sample type	Serum/EDTA plasma
Incubation time	29 min
Direct measurement	11.8 ...3 000 ng/mL
Measuring range with automatic dilution	11.8 ...1000 000 ng/mL
Detection limit	11.8 ng/mL
Kit stability on board	29 days
Calibrator	1 point
Calibration stability	15 days

Thermo Scientific B·R·A·H·M·S NSE KRYPTOR

Article number: 821.050

Assay characteristics

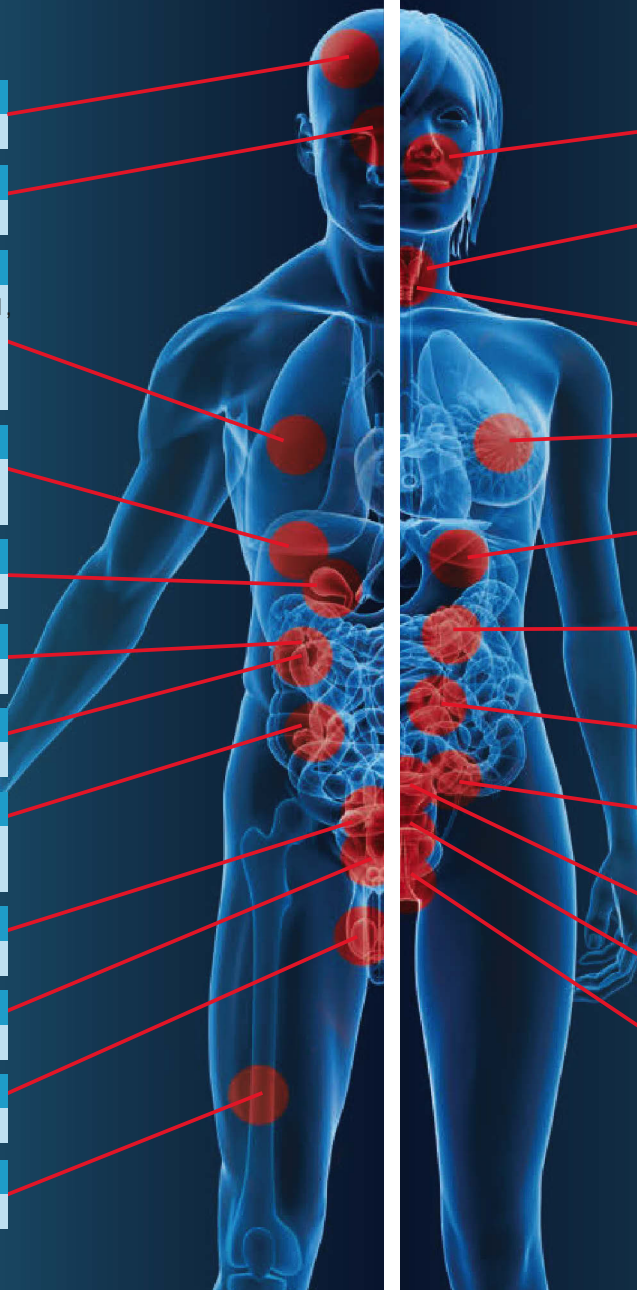
Determinations	50
Sample volume	70 µL
Sample type	Serum
Incubation time	59 min
Direct measurement	0.8 ... 200 ng/mL
Measuring range with automatic dilution	0.8 ... 10 000 ng/mL
Detection limit	0.8 ng/mL
Kit stability on board	15 days
Calibrator	2 points
Calibration stability	15 days

References

1. Bajetta E et al. Chromogranin A, neuron specific enolase, carcinoembryonic antigen, and hydroxyindole acetic acid evaluation in patients with neuroendocrine tumors. *Cancer* 1999; 86: 858-65
2. Inman Z et al. Automated Chromogranin A: Is KRYPTOR the way to go? AACB Meeting 2012 Melbourne, Poster P85
3. Lawrence B et al. The clinical relevance of chromogranin A as a biomarker for gastroenteropancreatic neuroendocrine tumors. *Endocrinol Metab Clin North Am* 2011; 40(1): 111-34
4. Modlin IM et al. Chromogranin A -Biological function and clinical utility in neuroendocrine tumor disease. *Ann Surg Oncol* 2010;17(9): 2427-43
5. Tapia FJ et al. Neuron-specific enolase is produced by neuroendocrine tumours. *Lancet* 1981; 1: 808-11
6. Trapé J et al. Increased plasma concentrations of tumour markers in the absence of neoplasia. *Clin Chem Lab Med* 2011; 49(10): 1605-20
7. Vezzosi D et al. Chromogranin A measurement in metastatic well-differentiated gastroenteropancreatic neuroendocrine carcinoma: screening for false positives and a prospective follow-up study. *Int J Biol Markers* 2011; 26(2): 94-101

**Thermo Scientific
B·R·A·H·M·S Tumor Markers**
A broad range of markers available

Brain	NSE, CEA
Pituitary Gland	Prolactin
Lung	SCLC: NSE, CYFRA 21-1, Chromogranin A NSCLC: SCC, CYFRA 21-1, CEA
Liver	AFP, CEA, CA 19-9, Chromogranin A
Gallbladder	CA 19-9, CEA
Adrenal Gland	Chromogranin A
Kidney	CEA, NSE
Colon	CEA, CA 19-9, Chromogranin A
Bladder	CYFRA 21-1, CEA, NSE
Prostate	Total PSA, Free PSA
Testicle	AFP, hCG+ β
Bone Metastases	Osteocalcin



ENT (Ear, Nose, and Throat)	SCC, CYFRA 21-1, CEA
Thyroid	MTC: Calcitonin, Chromogranin A, CEA DTC: Thyroglobulin, CEA
Esophagus	SCC, CYFRA 21-1, CEA
Breast	CA 15-3, CEA
Stomach	CEA, CA 19-9, Chromogranin A
Pancreas	CA 19-9, CEA, Chromogranin A
Neuroendocrine Tumors	Chromogranin A, NSE
Ovary	CA 125 II, CEA, AFP, hCG+ β
Uterus	SCC, hCG+ β , CYFRA 21-1
Cervix	SCC, CYFRA 21-1, CEA
Vagina, vulva	SCC

Clinical Diagnostics

Thermo Fisher Scientific
B·R·A·H·M·S GmbH
Neuendorfstr. 25
16761 Hennigsdorf
Deutschland

+49 (0)3302 883 0
+49 (0)3302 883 100 Fax
info.onco@thermofisher.com
www.thermoscientific.com/brahms

Find out more at thermoscientific.com/brahms

©2017 Thermo Fisher Scientific Inc. All rights reserved.
All trademarks are the property of Thermo Fisher Scientific and its subsidiaries unless otherwise specified. KRYPTOR is a trademark of CIS bio international, licensed for use by B·R·A·H·M·S, a part of Thermo Fisher Scientific.

Thermo Fisher Scientific products are distributed worldwide; not all intended uses and applications mentioned in this printing are registered in every country.