Prospective randomized multicenter comparison of indocyanine green (ICG)-99mTc-nanocolloid vs. 99mTc-nanocolloid plus an intraoperative injection of ICG for the detection and surgical resection of the sentinel nodes in patients with prostate cancer

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Primary Objective(s): 1. Number of positive patients (as determined following histopathological analysis of the excised nodes).Secondary Objective(s): Collection of the below summarized information will provide us an answer to the following...

Ethical review	Approved WMO
Status	Pending
Health condition type	Reproductive neoplasms male malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON45195

Source
ToetsingOnline

Brief title
Free vs nanocolloid bound ICG for prostate sentinel node

Condition

- Reproductive neoplasms male malignant and unspecified
- Prostatic disorders (excl infections and inflammations)

Synonym

prostate cancer, prostate carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: Karl-Storz,Storz

Intervention

Keyword: node dissection, prostate cancer, prostatectomy, sentinel lymph node

Outcome measures

Primary outcome

Number of positive patients (as determined following histopathological

analysis of the excised nodes).

Secondary outcome

Collection of the below summarized information will provide us an answer to the

following secondary endpoints:

1. What is the role of preoperative SPECT/CT for the identification of SNs

draining from the prostate?

2. Is there a difference between ICG-99mTc-nanocolloid and free ICG in the

optical identification of SNs of the prostate?

Study description

Background summary

Sentinel node (SN) identification was shown to aid in the diagnosis of nodal metastases in prostate cancer. Since the introduction of lymphoscintigraphic SN detection for prostate cancer by Wawroschek and collegues [Wawroschek et al., Eur Urol 1999] several institutes showed the value of SN for detecting nodal metastases outside the field of the extended nodal dissection. Despite this

improved diagnosis, SN dissection has not gained widespread acceptance. Several explanations for the absence of SN detection in daily practice can be put forward. The false negative rate of SN detection, that is the percent of men that have lymph node metastases despite a negative SN procedure, ranges between 5 and 15% with a mean op 10% (Table 1). This can be explained by inadequate drainage of tracer into lymph nodes due to tumor infiltration or lymph tract blockage by tumor. It can also be explained by the inability to properly detect and resect the SN(s) during the surgical procedure.
The complexity of lymph drainage for pelvic organs such as bladder and prostate requires thorough mapping of the draining lymph nodes, such as SN in both the pre- and intraoperative setting. Classically, this imaging was performed for penile cancer using lymphangiography [Cabanas, Cancer 1977]. Lymphoscintigraphy was introduced in the 90s of the last century, and later the introduction of single photon emission tomography complemented with computer tomography scanning allowed the nuclear mediciny physician to localize the SN(s) within its anatomical habitat.
For intraoperative detection a gamma probe-based detection method can be applied. Although highly sensitive, gamma probe detection has a low spatial resolution and cannot distinguish between the area of interest and the background signal (coming from the prostate) in case a SN is located close to the prostate. Since gamma ray detection provides no anatomical detail and blue dye was shown to be of little value, recently fluorescent dyes (e.g. indocaynine green (ICG)) were introduced in for intraoperative SN detection [Polom et al., Cancer 2011; van den Berg et al., J Nucl Med 2013; Jeschke et al., Urology 2012]. Next to free ICG, we introduced the hybrid tracer (ICG-99mTc-nanocolloid) combining radioactivity and fluorescence for the detection of the SN [van Leeuwen et al., J Biomed Opt 2011]. With this hybrid tracer, in prostate cancer patients we showed that it allowed for both preoperative SN mapping and intraoperative gamma ray detection using the radioactive signature of this tracer. In addition, the fluorescence signature provided intraoperative near infrared (NIR) fluorescence-based detection of the SN(s) [van der Poel et al., Eur Urol 2011].
As compared to dissection based on the acoustic signal provided by the gamma probe, NIR-guided SN dissection allowed for more accurate identification of the individual SN and also provided anatomical information on lymph tracts [Jeschke et al., Urology 2012]. However, in contrast, the use of the fluorescent dye alone does not allow for preoperative SN mapping and as such discriminating SNs from non-SNs (higher-echelon nodes) can become difficult.
Several questions remain on the value of ICG-NIR guided SN identification. The role of the local tracer injection into the prostate is more important than previously assumed (J Nucl Med. 2012 Jul;53(7):1026-33.). Moreover, the additional value of intraoperative ICG-NIR tracing of the ICG signal over the conventional approach of aboveof gamma signal tracing needs evaluation. In addition, as well as the role of free ICG versus 99mTc-nanocolloid bound ICG (ICG-99mTc-nanocolloid) should be evaluated to determine the value of the tracers. Free ICG more rapidly migrates from the prostate into both lymph tracts and nodes, but does not accumulate for longer periods into

the nodes. In contrast, the hybrid tracer ICG-99mTc-nanocolloid Nanocolloid is transported slower throughin the lymph system and like free ICGits parental compound 99mTc-nanocolloid it accumulates in the SN [Uren, Ann Surg Oncol 2004]. (Uren, Howman-Giles, & Thompson, 2003) Similar to free ICG the nanocolloid is transported to second tier nodes in case of a saturated SN, as does nanocolloid bound ICG.
To address these important questions we designed a prospective randomized multicenter study to compare the hybrid tracer (ICG- 99mnanocolloid-bound Tc-nanocolloid) and freeto ICG for sentinel node biopsy in prostate cancer as well as the efficacy of NIR-based guided SN tracing over compared to 99mTc99m gamma signal tracing will be determined.

Study objective

Primary Objective(s):
1. Number of positive patients (as determined following histopathological analysis of the excised nodes).

Secondary Objective(s):
Collection of the below summarized information will provide us an answer to the following secondary endpoints:
1. What is the role of preoperative SPECT/CT for the identification of SNs draining from the prostate?
2. Is there a difference between ICG-99mTc-nanocolloid and free ICG in the optical identification of SNs of the prostate?

Study design

Prospective randomized case-control study.

Intervention

Approximately 4 hours prior to surgery ICG-99mTc-nanocolloid will be injected transrectally under ultrasound guidance into the prostate as is routinely done for 99mTc-nanocolloid guided sentinel node detection. Patients will undergo lymphoscintigraphy and a SPECT/CT scan for preoperative planning. In group 2 the patients will receive an intraprostatic injection 10 minutes prior to the prostatectomy and sentinel node detection.

Study burden and risks

Other than intraoperative injection and tracking of ICG, this study will not be any different from standard procedures. ICG-99mTc-nanocolloid will be injected approximately 4 hours prior to surgery. It may, however, be anticipated that the number of resected sentinel nodes, and hence staging, may be improved after ICG-99mTc-nanocolloid injection. As mentioned earlier, in rare cases

oversensitivity: nausea, urticarial and anaphylactic reactions (< 1/10.000 (ICG) have been reported after intravenous injection of ICG. Patients will be monitored up to 24 hours post-surgery. Conversely, the value of adequate staging could have major results on the improvement of staging and postoperative outcome of prostate carcinoma patients.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Histologically proven prostate cancer;
• Patients are clinically node negative and metastases negative (N0, M0);
• Increased risk of nodal metastases according to the Briganti nomogram (> 7%);
• Scheduled for surgical (laparoscopic or robotic) prostatectomy including nodal dissection.

Exclusion criteria

• History of iodine allergy;
• Hyperthyroid or thyroidal adenoma;
• Kidney insufficiency.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2015
Enrollment:	50
Type:	Anticipated

Ethics review

Approved WMO Date:	28-02-2014
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	29-01-2016
Application type:	Amendment

Review commission: METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL46580.031.13