MultiSPectral fLuorescence Imaging as a Tool to separate healthy and disease related lymphatic anatomies during lymph node dissections in prostate cancer.

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We aim to evaluate the technical feasibility of imaging two different lymphatic drainage profiles, namely that of healthy tissue (i.e. the lower limbs/abdominal wall) and that of the primary tumor (i.e. prostate). To realize the differentiation,…

Ethical review	Approved WMO
Status	Completed
Health condition type	Reproductive neoplasms male malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON54192

Source
ToetsingOnline

Brief title
SPLIT study

Condition

- Reproductive neoplasms male malignant and unspecified

Synonym
Prostate cancer

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: NKI-AVL

Intervention

Keyword: lymph node dissection, Multispectral lymphatic imaging, Prostate cancer

Outcome measures

Primary outcome

- Determine the technical feasibility of using multispectral fluorescence imaging to distinguish between two lymphatic drainage patterns LNLower limb/abdominal wall (fluorescein) and LNprostate (ICG-99mTc- nanocolloid)) in prostate cancer patients scheduled for RALP + ePLND + SN us-ing the Firefly Si laparoscope (da Vinci Si®) and/or Image 1 HUB HD + D-light P (Karl Storz) system.

- Determine whether and where the lymphatic drainage profile of the lower limbs/abdominal wall converge with the drainage profile of the primary tumor: are there lymph nodes containing both fluorescein and ICG-99mTc- nanocolloid

Secondary outcome

- Correlate pathological tumour findings in the excised nodal specimens with the presence of ICG-99mTc- nanocolloid or fluorescein (or lack thereof) in order to assess if separation of the lymphatic drainage pathways in fact also means that no metastases are found in LNLower limb/abdominal wall (fluorescein).

- Determine whether fluorescein is also found in lymph nodes in ePLND template on contralateral side of injection in lower limb/abdominal wall

- Determine the anatomical relationship between the lymphatic drainage profile

of the lower limbs/abdominal wall and the sentinel node of the primary tumor

- Determine lymph fluid leakage by measuring this during surgery as this can be

a predictive factor for complications:

o Leakage yes/no?

o Yes: <1cm from lymphnode?

o Yes: >1cm from lymphnode?

*

Study description

Background summary

We hypothesized that real-time multispectral fluorescence imaging of both the lymphangiographic tracer fluorescein and the SN specific tracer ICG-99mTc-nanocolloid is technically feasible and will allow us to differentiate the lymphatic drainage profiles of healthy tissues, i.e. those of the lower limbs (fluorescein) from those of the primary tumour (ICG-99mTc-nanocolloid), respectively (Figure 1). The potential of this concept was previously evaluated in male pigs (n = 5) (Meershoek et al. JNM 2018; Meershoek et al. JRS 202021,22). Here, the lymph nodes that drained the lower limbs were differentiated from the lymph nodes that drained the prostate. Uniquely, no overlap could be observed between the lymphatic drainage pathways. The chance of complications for ePLND vs limited PLND is much higher (OR = 2.118, 95% CI: 1.107*4.051, z = 2.27, P*= .023) (Zheng et al, prec. Med. Sciences 2020)23, and is related to the number of lymph nodes resected. In Rousseau et al. (prog urol. 2014) it is suggested that sparing the lateral side of the iliac artery at the lateral dissection reduced risk of lymphatic complications without decreasing metastasis detection rate24. Hence, we feel that we are obliged to study whether in the future non-tumor-associated lymph nodes i.e. of the lower limbs, in humans can remain in situ.

Study objective

We aim to evaluate the technical feasibility of imaging two different lymphatic

drainage profiles, namely that of healthy tissue (i.e. the lower limbs/abdominal wall) and that of the primary tumor (i.e. prostate). To realize the differentiation, real-time multispectral fluorescence imaging of two spectrally different tracers (the lymphangiographic tracer fluorescein (injected in the lower limbs and abdominal wall) and SN specific tracer ICG-nanocolloid (injected in the tumor)) will allow for multispectral (or multicolor) fluorescence imaging.

Study design

An investigator initiated, prospective, non-randomized, feasibility study.

Study burden and risks

Group A: The injection of fluorescein in the lower limb(s) is the only deviation from existing procedures (in prostate cancer the use of ICG-99mTc-nanocolloid has already been evaluated in 452 patients at the NKI. A previous study using intraprostatic administration of both fluorescein and ICG-99mTc-nanocolloid in the same patient has shown that the use of fluorescein does not expose the patients to any additional risk (vd Berg et al., Eur Urol 2017 (n=10))1. A negligible risk involved with participation are allergy towards fluorescein or ICG. Fluorescein comes as a slightly basic compound. This could cause a stinging feeling when injected, which is why this is done when the patient is under general anaesthesia starting with 1:5 dilution with saline 0.9%. Both compounds are clinically approved, have been extensively used in humans and their allergy profile has been specified. Of important note, the dissection templates of the ePLND procedure will not be changed for this study and only additional SN*s identified via ICG-99mTc-nanocolloid will be resected (as has been done previously in n=452). The urine and the skin at the injection site may remain coloured for up to 2 days after injection. In Chang et al., Asian. J. surg. 2019, no anaphylaxis and no cases of skin necrosis at injection site were observed2.

Group B: The injection of ICG in the abdominal wall is the only deviation from existing procedures.

There are no other burdens. The benefit of the study is that insight into the lymphatic anatomy may in the future lead to less invasive procedures that spare lymphatic structures that are not related to the primary tumor and as such reduce the toxicity and complications of PLND. Key herein is that the oncological outcome is preserved.

Contacts

Public
Antoni van Leeuwenhoek Ziekenhuis

Plesmanlaan 121
Amsterdam 1066CX
NL
Scientific
Antoni van Leeuwenhoek Ziekenhuis

Plesmanlaan 121
Amsterdam 1066CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Male, aged >= 18 years.
* WHO performance status 0,1, or 2.
* Written informed consent.
* Histopathologically confirmed adenocarcinoma of the prostate
* Increased risk of nodal metastases according to the MSKCC nomogram (> 7%)
* Scheduled for surgical (laparoscopic) prostatectomy including ePLND
* Suitable for RP and ePLND, as per institutional guidelines

Exclusion criteria

* Prostate cancer patients with prior abdominal or inguinal surgery
* History of allergy to iodine, food or medicinal induced urticaria, asthma, eczema, or aller-gic rhinitis
* Hyperthyroid or thyroidal adenoma

* Kidney insufficiency
* History of oversensitivity to FLUORESCITE composites
* Patients using beta-blockers

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	24-03-2022
Enrollment:	28
Type:	Actual

Ethics review

Approved WMO

Date:	28-10-2021
Application type:	First submission
Review commission:	METC NedMec

Approved WMO

Date:	11-05-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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
ClinicalTrials.gov	NCT05120973
CCMO	NL78523.031.21

Study results

Date completed: 24-07-2024

Results posted: 17-12-2024

First publication
12-10-2024