Prediciting Radiation-Induced lung injury through patient-specific lung epithelial ORganoids

Published: 08-12-2020
Last updated: 08-04-2024

To demonstrate the validity of using patient-derived lung epithelial organoids, as a model of normal lung tissue, we aim to assess lung epithelial cell responses to ionizing radiation exposure and relate these to clinical outcome. In addition,...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON52503

Source
ToetsingOnline

Brief title
PRIOR

Condition

- Other condition
- Respiratory tract neoplasms

Synonym
Radiation damage, Radiation induced lung damage, Radiation Induced Lung Injury

Health condition

Pulmonale fibrose en pneumontis na radiotherapie

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: biomarkers, NSCLC, Radiation Induced Lung Injury, Radiotherapy

Outcome measures

Primary outcome

A significant difference in the number of *H2AX foci (double strand DNA damage) per cell induced by in vitro radiation between patient-specific normal epithelial cells from patients with * grade 2 pneumonitis or fibrosis following chemoradiation or proton therapy based on CTCAE scoring system and patients with grade * 1 pneumonitis or fibrosis.

Secondary outcome

In vitro:

* Measurement of in vitro-induced changes in EMT (e.g. TGF-beta, alpha-SM-actin, SLUG, vimentin), -oxidative stress (e.g. HMOX1), or -inflammation (e.g. IL-6) by ionizing radiation in normal lung epithelial cell cultures derived from bronchoalveolar lavage fluid.

Changes in the following clinical parameters following radiation:

* Performance, symptoms and QOL as measured by questionnaires;

* Lung function (VC, FVC, FEV1) and diffusion capacity (DLCOc, KCO);

* Respiratory resistance (Rrs) and reactance (Xrs) as measured by forced oscillation technique;

* Lung structure as measured by CTCAE grading on CT thorax;

* Lung density measured by quantitative densitometry using CT-thorax.

- The *-H2AX decay ratio in peripheral lymphocytes by measuring the difference

in foci at 30 min and 24 hours after 1Gy radiation of peripheral lymphocytes.

Study description

Background summary

Standard of care for patients with stage III non-small cell lung cancer (NSCLC) is chemotherapy combined with concurrent or sequential radiotherapy. Radiation-induced lung injury (RILI) of normal lung tissue is one of the main dose-limiting factors during radiation treatment. Therefore, it is important to identify which patients are at risk for RILI to be able to create a personalized radiation treatment and prevent reduction in quality of life (QOL) in cancer survivors. So far, no reliable biomarkers have been found that can be used for this identification. This study aims to use patient-derived airway epithelial organoids to search for individual predictors for RILI.

Study objective

To demonstrate the validity of using patient-derived lung epithelial organoids, as a model of normal lung tissue, we aim to assess lung epithelial cell responses to ionizing radiation exposure and relate these to clinical outcome. In addition, clinical outcome parameters will be combined to create a better understanding of RILI.
Study design: This study is a prospective cross-sectional study.

Study design

This study is a prospective cross-sectional study.

Study burden and risks

The eligible patient group has a severe disease with an intensive treatment regimen. However, since the burden and risk of the measurements is low and the possible outcome of this study may benefit future patients with comparable disease, we have concluded that the benefit-risk ratio is acceptable. Most measurements are part of standard clinical care and follow-up. Additional measurements are questionnaires, lung function and additional low-dose CT images at baseline and 3 times after that. Bronchoalveolar lavage will be added to a planned diagnostic procedure under sedation, therefore not giving additional burden to the patient. It has a minimal risk of fever, bleeding or

bronchospasm, none requiring specific therapy.

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333ZA
NL
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333ZA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

* Age * 18-85 years;
* Clinical suspicion of lung tumor with mediastinal lymph node involvement based on enlarged lymph nodes on CT thorax or FDG uptake on PET-CT conform ESMO guidelines;
* Planned bronchoscopy with endobronchial ultrasound (EBUS) with sedation (Propofol or benzodiazepine) for standard diagnostic work-up;
* Clinical performance adequate for undergoing EBUS (according to pulmonary physician ordering the diagnostic procedure).

Exclusion criteria

* Clinical performance too low to undergo EBUS according to pulmonary physician ordering the diagnostic procedure;
* Suspicion of metastasis or stage IV disease on PET-CT or CT-thorax;
* Inadequate understanding of the Dutch language in speech and writing.
* Clinical performance too low to receive chemoradiotherapy or proton therapy;
* Significant co-morbidities such as end stage renal disease, severe cardiovascular disease, severe psychiatric disease, end stage COPD, or other comorbidity with limited expected survival (<1 year) or WHO performance status >3
* Known pre-existent diagnosis of lung fibrosis or newly diagnosed lung fibrosis before start of the study;
* Previous thoracic radiation-treatment.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	16-02-2021
Enrollment:	65
Type:	Actual

Ethics review

Approved WMO

Date:	08-12-2020
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

	metc-ldd@lumc.nl
Approved WMO Date:	09-12-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	28-06-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL73109.058.20