CORAL: Community in Oncology for Rapid Learning

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Philippe Lambin
Simone Moorman
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Agenda

- Introduction round (10 min)
- Overview of Rapid Learning projects (20 min, Andre, Philippe)
- Desire and need (or not) to build a community (10 min, Vincenzo)
- Clinical applications (10 min, Corinne)
- Wrap-up and next steps (10 min, Simone)
Housekeeping

• Slides and contact details of people present will be shared with the group
• Unless you object (let Andre know)
Introduction Round
Introduction

• Name, centre, background
• Your reason for coming to this meeting
• 30 seconds
Overview of Rapid Learning projects
UKCAT

**Reported by:** Corinne Faivre-Finn (The Christie and University of Manchester)

**Funding:** Cancer Research UK Major Centre. Aiming for programme grant

**Period:** 2015-2020

**Staff:** RRR clinicians, physicist, data manager, project manager, statistician, bioinformatician

**Platform:** Various open source components, own developments

**Patient group(s):**
- Lung Cancer (e.g., elderly, 90 day mortality, cardiac toxicity)
- CNS
- Gynae
- Prostate

**Deliverable(s):**
- Outcome prediction models
- Integration of biomarkers (circulating biomarkers and radiogenomics)
Christie CAT system update

**Data mining**
- Prospective RT plan collection
- Nightly sync to institution clinical systems
  - Clinical Web Portal (eRecords)
  - Mosaiq
- On demand data upload (sql selection of patient cohort)
  - Clinical PACS
  - IGRT (XVI) nearline archive
- Upload of Clinical trial DBs
- Retrieval from archive
  - Pinnacle RT plans (2008 onwards)
  - IGRT DBs and images

**Data analysis**
- Christie Image Analysis Pipeline
  - Volumetric/dosimetic parameters (validated)
- In development
  - IGRT change parameters
  - Basic radiomic image analysis

**Distributed learning**
- Basic parameter D2RQ scripts for CatDB -> RDF store data dump
- Development of comprehensive D2RQ scripts against ROO/
- Sesame end point functioning
- Awaiting distributed learning application
Christie CAT projects (some examples)

**PhD Patient change in IGRT**
- Do changes in patients observed in IGRT data increase accuracy of predictive models?
  - Random Forest base model
  - Inclusion of 4D (ITV) parameters in 3D (GTV) models
- Patient motion
- Tumour response

**GBM outcome prediction**
- Overall survival
- Original Christie model (inc dosimetric parameters)
- Collaboration with Maastro clinic providing validation cohort (in progress)

**GBM radiomics**
- Does radiomics add prognostic value in GBM outcome prediction?
- Collaboration with Maastro clinic
- Software transfer agreement for radiomics software in progress

**Lung dysphagia**
- Bayesian Network oesophagitis prediction
- Collaboration with Maastro clinic
- 280 Christie patient validation cohort

**Prostate outcome prediction**
- Survival model
- Collaboration with Maastro clinic
- 2770 Christie patient validation cohort

**Natural Language Processing**
- Extraction of toxicity data from historical medical notes
- Initial oesophagitis training dataset

**GBM retrospective biomarker aggregation**
- Retrospective analysis of tissue bank samples from previously treated GBM patient cohort
- Seeking funding (applications made)

**Metastatic brain SRS**
- Overall survival
- Collaboration with Maastro clinic
# Projects (MAASTRO)

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Various open source components, own developments & Varian learning portal Outcome prediction models
ozCAT

Reported by: Lois Holloway, David Thwaites
Funding: NSW Ministry of Health + Trust funding
Period: 2014-

Participating site(s):
• Liverpool & Macarthur CC, Liverpool, Australia
• ICCC, Wollongong, Australia
• Westmead Hospital, Westmead, Australia
• Calvary Mater, Newcastle, Australia
• More sites tentative (Western Australia, Victoria)
• MAASTRO, Maastricht, Netherlands

Platform:
• Fully open source

Patient group(s):
• Lung cancer, head & neck, prostate cancer

Deliverable(s):
• Outcome prediction models
Strategy/BIONIC

Reported by: Andre Dekker, MAASTRO
Funding: STW-NOW-Deity (IndoDutch joint funding)
Period: 2016-
Participating site(s):
• Tata Memorial, Mumbai, India
• Radboud UMC, Nijmegen, NL
• UMCG, Groningen, NL
• Erasmus MC, Rotterdam, NL
• MAASTRO, Maastricht, NL
Platform:
• Various open source components & own developments
Patient group(s):
• Various
Deliverable(s):
• Image learning – Distributed Radiomics
SAGE-ROO

Reported by: Andre Dekker, MAASTRO
Funding: Varian Medical Systems
Period: 2013-now
Participating site(s):
• MAASTRO, Maastricht, Netherlands
• UCSC, Rome, Italy
Platform:
• Various open source components, own developments & Varian learning portal
Patient group(s):
• Non specific
Deliverable(s):
• Quality enhancement tools & Dashboard
Reported by: Philippe Lambin, MAASTRO
Funding: EC, KWF
Period: 2016-2019
Participating site(s):
• MAASTRO, Maastricht, Netherlands
• Amsterdam, (VU/VUMC, NKI/Avl)
• Utrecht (UMCU)
• Azienda Ospedaliero Universitaria Di Parma (AOP)
• Heinrich-Heine Duesseldorf (UDUS)
• Fondazione IRCCS Istituto Nazionale dei tumori Milano (INT)
Platform:
• Delta-Radiomics + genetic
Patient group(s):
• Head and neck cancer patients treated with (chemo)-radiotherapy, surgery
Deliverable(s):
• Mutifactorial Decision Support System integrating genetics + individualized patient decision aids
**Reported by:** Philippe Lambin, MAASTRO  
**Funding:** Eurostars  
**Period:** 2016-2018  
**Participating site(s):**  
- MAASTRO, Maastricht, Netherlands  
- Radboud  
- Others?  
**Platform:**  
- Delta-Radiomics  
**Patient group(s):**  
- Lung cancer patients treated with radiotherapy, chemotherapy and immunotherapy  
**Deliverable(s):**  
- Early biomarkers of outcome
MitoTx

Reported by: Philippe Lambin, MAASTRO
Funding: DNAmito, KWF
Period: 2016-2019
Participating site(s):
• MAASTRO, Maastricht, Netherlands
• Royal Marsden, UK
Platform:
• Genetics (mtDNA, nDNA)
Patient group(s):
• Breast cancer patients treated with (chemo)-radiotherapy, surgery
Deliverable(s):
• mtDNA signature
• Mutifactorial Decision Support System integrating genetics
Desire and need for a community?
Why a community

• We need to grow from 20 to 2000 centres if we really want this rapid learning thing to work
• We need to reuse results and tools across scattered projects (Learn Rapid Learning)
• We need a radiation oncology approach to inform other approaches (e.g. ASCO’s CancerLinq)
• Without a community we run the risks of getting silo’s (e.g. a Varian silo or a MAASTRO silo)
• Often we get questions “Do you have a validation set for model X”, we need to know who has what and with which quality
Why **not** a community

- We don’t want to be a select club
- We need to be inclusive
- An umbrella (e.g. ESTRO/ASTRO/...) is going to give resistance
- We want to speed up the Rapid Learning idea not slow it down
- Membership may not offer enough benefits, we need to invest first
- We have enough meetings already
What would CORAL look like

• Meeting point for data providers, researchers and clinicians

• Sub-communities
  • Data
  • Models
  • Clinical applications
Communities inside CORAL

• Data
  • Organize the entrance of new data providers
  • Get new providers started at minimal cost for them
    • Search for funding
    • Limited cost tools
      • Small footprints (no heavy IT needed)
  • Help centres get IRB approval
• Catalogue
• Govern the ontology
• Make sure all data providers are using the same ontology and data syntax
Communities inside CORAL

• Modelling
  • Get new researchers started
    • Search for funding
    • Connect them to data providers
  • Open code repository for quick start
    • Learning tools
    • Validation tools
• Sharing models
• Define/share best practices (e.g. TRIPOD)
• User friendliness of Rapid Learning
• Launch disruptive ideas (e.g. Radiomics)
Communities inside CORAL

• Clinical Applications
  • Develop umbrella protocols / CDEs
  • Catalogue models and their quality
  • Define methodology for testing models in the clinic
  • Set-up clinical trials with models
  • Get evidence for Rapid Learning
What do you think?

- Would a community be beneficial for you?
- What type of member would you be?
  - No member
  - Passive (listening in, keeping yourself up to date, using the final results if evidence is there)
  - Active (providing data, doing research, joining clinical trials)
- Would you prefer the community to be
  - Affiliated
  - Non-affiliated
Clinical applications
The need to provide evidence to support the routine use of models
RT clinical trials have been hampered by difficulties relating to

- Selection bias (e.g., elderly are excluded)
- Slow and poor accrual
- Lack of power
- Failure to incorporate novel data as knowledge evolves during recruitment time
  - RT technology
  - Biology of cancer
1-Need for predictive models

Potential for the Continuous Clinical Trial
Learn from every patient treated in the routine setting

2-Need for clinical application

To accelerate the dissemination of new knowledge into the routine care of patients with cancer
Prediction of oesophageal toxicity
Maastro clinic - Nomogram

Points

age

overall treatment time

mean esophagus dose

max esophagus dose

timing chemotherapy

gender

WHO-PS

Total Points

Prob dysphagia≥2

Prob dysphagia≥3
Doctors’ prediction of radiation oesophagitis

- Prospective study (n=137)
- 5 clinicians
- After first visit of patients to the RT department physicians were asked to predict the probability of acute severe dysphagia (≥grade 3)

Performance on MAASTRO validation set (n=137)

- model AUC = 0.78
- doctors AUC = 0.53

P=0.012

Dehing-Oberij. Radiother Oncol 2010
The need
Design novel stratified medicine trials using validated RT outcome prediction models

• Development of decision support systems (DSS) that are patient friendly inc web tools/apps…
• Qualitative research to ascertain whether patients would be willing to be randomised on the basis of DSS
• Prospective multi-centric randomised phase II/III clinical trial to evaluate if use of models lead to better outcome
  Example-optimal treatment for good PS stage III elderly patients
    • Current standard of care (conc CTRT)
    • DSS-informed practice based on toxicity (eg oesophagitis/fatigue) and survival (inc short term and long term mortality)
      • Low risk early mortality and toxicity→conc CTRT
      • High risk early mortality and toxicity→seq CTRT/RT alone
DESSERT: Study Design

- Option 1 – submitted design
  - Prospective cohort study
  - Implement DSS for all eligible patients
  - Measure outcomes and compare with control group treated up to 3y preceding

- Option 2
  - Cluster randomised trial
  - Randomise centres to DSS or not and compare outcomes

- Option 3
  - Randomised control trial
  - Randomise clinicians to DSS or not and compare outcomes
DESSERT: Study Design

DSS 1
Determine prognostic group

- Good Prognosis: DSS informed curative RT
- Poor/Medium Prognosis: DSS informed palliative RT

DSS 2
Toxicity
Wrap-up and Next Steps
Next steps

• Think big, start small, act now
• [http://www.eurocat.info/v2/info.html](http://www.eurocat.info/v2/info.html)
• Share slides of this meeting
• Start a web(site) based community – refactor euroCAT site
  • Subscription
  • List of associated partners and projects
• Repeat at ASTRO with North American centres
• Data sub-community (tcon to setup)
  • Joint paper on the ROO
• Clinical Application sub-community (tcon to setup)
  • One-day workshop to figure out trial designs