Personalised Medicine, Cancer and Artificial Intelligence

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Why do we need AI in cancer care?

- Cancer is a disease of the elderly
- There is already a *population time bomb*
- Health care has become unaffordable in many countries
- Out only hope is new technology.....
Global Burden of Cancer

• Cancer kills more people each year than AIDS, TB, and Malaria put together
  (WHO 2009)
Divergence between high & low-middle income

- Double & triple disease burden impacting aged populations
- Impact of globalization
- Conflict & de-development
- Demographic challenges (dependency ratio)
Socially Deprived People

• Higher rate of cancer, obesity, smoking,
• Poorer detection rate, poor health communication.
• Inferior treatment, costs often prohibitive
• Much higher mortality (seen as early as one year)
• Co-morbidity- diabetes, cardiovascular events, Alzheimers
David, has returned to Italy this week after an amazingly successful 12 week UK tour sponsored by McDonalds.
Changing therapeutic geographies for ageing cancer patients
Intrinsic systemic weakness – historical impact of structural adjustment programs coupled to:

- Re-emergence of debt
- Political & governance failures
- Trade-offs between needs of young and old

Economist. *Public debt in Africa*. March 10th, 2018
Mexico, a traditionally strong public sector health system, has seen loss of 65-91% cancer services in cartel ‘narcowar’ areas. The elderly disproportionately impacted.

The challenge of cancer in middle-income countries with an ageing population: Mexico as a case study. eCancer 2015: 9 536-555.

Re-aligning cancer policy to make it pro-ageing
More intelligent onco-politics
EAPM Meeting 2014

Chairman
ONE SIZE DOES NOT FIT ALL
Personalised Medicine

• Patient centred
• Multidisciplinary in research (translational)
• Multidisciplinary in care delivery
• Fusion of data (protected) with validated AI tools
“The doctor will see you now—I can’t promise that he’ll talk to you, but he’ll see you.”
“Who is” the patient?
Different philosophies to approach personalised medicine

Philosophy (1):

1. Basic Research
2. Translational Research
3. Clinical Research
4. Patient
Different philosophies to approach personalised medicine

Philosophy (2):

Basic Research Scientists → Research on patient health or disease → Clinical Research Scientists

Translational Research Platforms & Other-discipline scientists
Putting the patient in the centre of personalised medicine

Patient

Basic Research Scientists

Research on patient health or disease

Clinical Research Scientists

Translational Research Platforms & Other-discipline scientists
Profiling the patient... (using an AI tool)

- Perceived health state
  - GSRH (2)
  - Pain (2)
  - Fatigue (3)
  - Physical abilities (4)
  - Appetite (1)

- Psycho-social aspects
  - Social abilities (3)
  - Financial problems (1)
  - Sexual problems (3)
  - Body image (3)

- Psychological aspects
  - Anxiety (2)
  - Depressive symptoms (4)
  - Self-efficacy (6)

- Cognitive aspects
  - Memory/Attention (5)
  - Rumination (4)
  - Cognitive closure (5)
Main Objective: to provide physicians information that make them able to tailor their intervention on the patients’ psychological characteristics

Info includes not only the genetic, biological and clinical characteristics of the patients, but also their psychological, cognitive and emotional aspects
Creating tools that help patients to cope with stress generated by the illness itself and by their therapeutic journey in general (including participation in clinical trials)

Main Objective: to develop (AI) tools that support patients in their everyday life, through stress and emotional regulation and social support
Patient Empowerment AI and confidentiality

• Informed consent: How should one time informed consent be handled to confirm patient understands the benefits and risks of conducting future not yet defined research to address new questions based on archived samples?

• Ethical considerations
  • Late stage disease
  • Genetic testing

• How to best protect data of individuals while making the results of clinical trials transparent and available to a broad range of investigators

• How to enhance collaboration and data sharing especially for ‘Big Data’
Personalised Medicine

- Whose data is it anyway?
- NHS sold data on 40million patients to Insurance industry for £2,200- NO PERMISSION, and CHEAP!
- Who trusts the scientists, doctors, insurance companies, Google Health??? THINK COVID19
- PLAN B Protected data input to make AI tools
- PLAN C— citizens’ cooperatives
HDC – A Federation of National HDC Cooperatives

- HDC Federation
- Common IT structure
- Common data storage in Switzerland
- Adapted to national healthcare systems
- Profits stay national HDCs
- A truly European solution
Each patient can exercise his/her right to choose a treatment if, and only if:

- (S)he is able to understand the available choice options
- (S)he is capable of expressing his opinion without fear of getting poorer treatment from irate medic!
Proposals should develop tools, platforms or services that will use information provided by most relevant diagnostic means for a particular area, resulting in an accurate, detailed, structured, systemic and prioritised assessment of the health status in a patient.

*in vitro* and/or *in vivo* diagnostics, medical imaging, -omics data, functional tests (lab-on-a-chip) etc.

The aim is to steer the development of solutions towards concrete patient and public sector needs, having the citizen and healthcare providers at the centre.
Molecular portrait of cancer
Personalised Healthcare in Oncology

ARTICLE

Signatures of mutational processes in human cancer

Signature of mutational processes in human cancer

Alexandrov et al. Nature August 2013

Cancer genome landscapes

Vogelstein et al. Science March 2013

TIME

HOW TO CURE CANCER

It's not a panacea - thanks to new genetic testing, the airliner-sized test of drug, treatment

Science
Personalised Medicine and Prevention (and Genes)

COGS identified 75 new susceptibility loci for mammary, ovary and prostate cancers

211,155 SNPs, ~200,000 patients; 1,000 scientists; 130 institutions
Public health implications

• Population Risk Stratification (risk-stratified screenings)
  
  24% fewer women need screening for breast cancer
  19% fewer men for prostate cancer at a cost of 3% and 4% missed cancers, respectively

• Personalised screening programme
  
  Individual genetic-risk assessment; Integration of genetic data with environmental, lifestyle and hormonal data; Personalized prevention plans (surveillance for early disease; lifestyle interventions; prophylactic chemoprevention)
Personalised Medicine

• From Genes and Lifestyle to ........
  Screening and Intervention of High Risk individuals
Genetic Signature-Prognosis of Breast Cancer

• 295 patients, Stage 1 or 2 disease, < 50yrs
• 70 gene profile on original tumour tissue
• Two groups followed to 10 years:
  • “Poor” vs “Good” 55% vs 95% survival
  • “Poor” vs “Good” 51% vs 85% DFS
• Better predictor than axillary node status
  (van de Vijver et al, 2002)
“The Anatomy Lecture of Dr. Nicolaes Tulp” – Rembrandt, 1632
The “normal profile” predicts Grade and Prognosis
Survival analysis was done on the 51 doxorubicin treated patients only

Sorlie, PNAS
Antibody-guided tumor targeting
Eligibility for Trastuzumab Therapy

HER2 status

- IHC
- FISH/CISH+
- Eligible for Trastuzumab

- FISH/CISH–
Joint Analysis: Disease-Free Survival: Addition of “H”

AC→TH→H

87%

N  Events
AC→T  1679  261
AC→TH  1672  134

HR=0.48, 2P=3x10^{-12}
HER2-positive breast carcinomas are exquisitely responsive to anthracycline-containing regimens

Topoisomerase 2 alfa co-amplification?


Test for interaction $\chi^2 = 13.7$, $p < 0.001$

Test for interaction $\chi^2 = 12.0$, $p < 0.001$
Trastuzumab inhibits the growth of human gastric cancer cell lines with HER2 amplification synergistically with cisplatin

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HER2 technical approaches

- **Gene amplification**
  - Southern or dot (slot) blotting
  - quantitative PCR
  - FISH/CISH/SISH

- **mRNA over-expression**
  - Northern blotting
  - quantitative RT-PCR

- **Protein over-expression**
  - immunohistochemistry
  - Western blotting
  - Elisa
We Are Getting Faster!!!
First- and second-generation tyrosine kinase inhibitors for cancer treatment

<table>
<thead>
<tr>
<th>Cancer type</th>
<th>Tyrosine kinase target</th>
<th>First-generation inhibitor</th>
<th>Second-generation inhibitor</th>
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<tbody>
<tr>
<td>Chronic myelogenous leukemia</td>
<td>BCR-ABL</td>
<td>Imatinib</td>
<td>Dasatinib</td>
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<tr>
<td>Gastrointestinal stromal tumors</td>
<td>c-Kit</td>
<td>Imatinib</td>
<td>Sutent</td>
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<td></td>
<td>PDGFR</td>
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<tr>
<td>Breast cancer</td>
<td>HER2</td>
<td>Trastuzamab</td>
<td>Lapatinib</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>EGFR</td>
<td>Erlotinib, Gefitinib</td>
<td>Irreversible inhibitors</td>
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<td>(EKB569)</td>
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1. **Minimally-invasive Surgical technologies**
technologies that decrease invasiveness and hospitalization (next generation robotics, HIFU, intraoperative radiotherapy, video-assisted surgery, mini-invasive surgery).

2. **Integrated Radiotherapy**
   *Hypofractionation*; integration with imaging (to improve our ability to identify the target) physics, chemistry and nanomedicine; loco-regional treatments (based on high precision radiation therapy techniques, ultrasound, radiofrequency, hyperthermia, mini invasive surgery, *radionuclide imaging and therapy*).

3. **Clinical molecular-imaging**
   including Radiochemistry, physics, PET and MRI for screening, early detection and treatment planning /monitoring

4. **Drug choice, response prediction and/or resistance**
Intra Operative Radiotherapy
(2,000 breast cancer patients)
Nipple-sparing with IORT

Irradiated area
Patient with bone marrow mets from a pancreatic G2 NET treated with PRRT with $^{177}$Lu-DOTATATE (25 GBq)
Possible targets for receptor radiotherapy

- oxytocin
- bombesin
- octreotide
- CCK/gastrin
- neurotensin
- & others ...
11C-Temozolomide.
Personalised Medicines

- Immunoncology, Antibodies, Vaccines, CarT cells
- Liquid biopsies, avatars
- Next next generation genomics
- Advanced high throughput screening
- High speed proteomics
- Integrated computational platforms
- Nanotechnology for oral medicines
- Management patient-centred, and IT monitored.
Outcomes
1972

No microwave ovens
No fax machines, Xerox copiers, PC’s
No internet or email, ATM’s, LCD’s
No CD’s, digital watches, mobile phones
No Northern/Western blots, PCR, DNA sequencing
No tumour suppressor genes, few oncogenes
No genes cloned, No Dolly
No NMR or PET scanners
No robotic endoscopy
No taxanes, interferons, interleukins
No GSF’s, imatinib

(after Meyskens, 2000)
Next 40 years-----

Exercise, diet, smoking, alcohol, Vaccines,
Screening (high risk)- video-pill, ’omics, robots and chemoprevention
Stem cells, Molecular imaging, Targetted R.T.
Individual care, Patient Empowerment
Education online
Cancer Image AI Datasets – eighteen to date

- Breast,
- Stomach,
- Brain,
- Cervix, Prostate
- Lymph nodes-Head and Neck
- Skin,
- Kidney, Liver
- Lung
‘omics Data Analyses in Cancer

• Early detection
• Prediction of prognoses
• Prediction of prognoses and chemoresistance
• Prediction of survival,
• Prediction of recurrence risk
• Microsatellite instability and survival
• Subtype analyses and clinical relevance
Outcomes from AI application to Cancer----
BIOMARKERS for improved patient care and QoL

• Choice of necessity, timing and extent of surgery
• Choice of dose, extent, modality, radiosensitisers, fractions of RT
• Need for neoadjuvant, adjuvant or primary use of medicines
• Single entity, cocktails, cytostatic, immune, vaccines, cells
• Schedule, dosage, route, interaction with RT, prediction of toxicity
• Eligibility for clinical trial
• Prediction of co-morbidity – cardiac, metabolic, neural
Outcomes of AI in cancer for Society

• Regulator approval
• Society belief! “A new Apple watch which cures cancer” NO WAY
• Doctor confidence- reliability in tools, replication, low cost
• Ease and speed of Health Assessment and decision making
• Language which patients, carers and doctors understand
• Less heterogeneity in outcomes for hospitals, regions and countries
• Healthcare funders- private and State
Personalised Medicine

Multimedia Communication
Leading cancer communication in Europe

- Information resource for professionals worldwide
- Peer to peer education and information
- Latest thinking delivered in an engaging format
District nurse put my father on death pathway - in his own home

NEEDLESS CANCER THERAPY FOR 4,000 WOMEN

A LETHAL ARROGANCE

For every life saved by breast screening, 3 patients undergo unnecessary treatment.
TIME

CANCER

Fact vs. Fantasy

A SPECIAL REPORT
TIME

There is new ammunition in the war against cancer. These are the bullets.

Revolutionary new pills like Celox combat cancer by targeting only the diseased cells. Is this the breakthrough we've been waiting for?

LUCIUS GURRISON GENERAL'S WARNING: Quitting Smoking. New study reveals serious risks to your health.

Marlboro

Come to where the flavor is.