Beacon Hospital Research Institute

Latest updates in Research and Clinical Trials

Prof. David Burke and Ailish Daly

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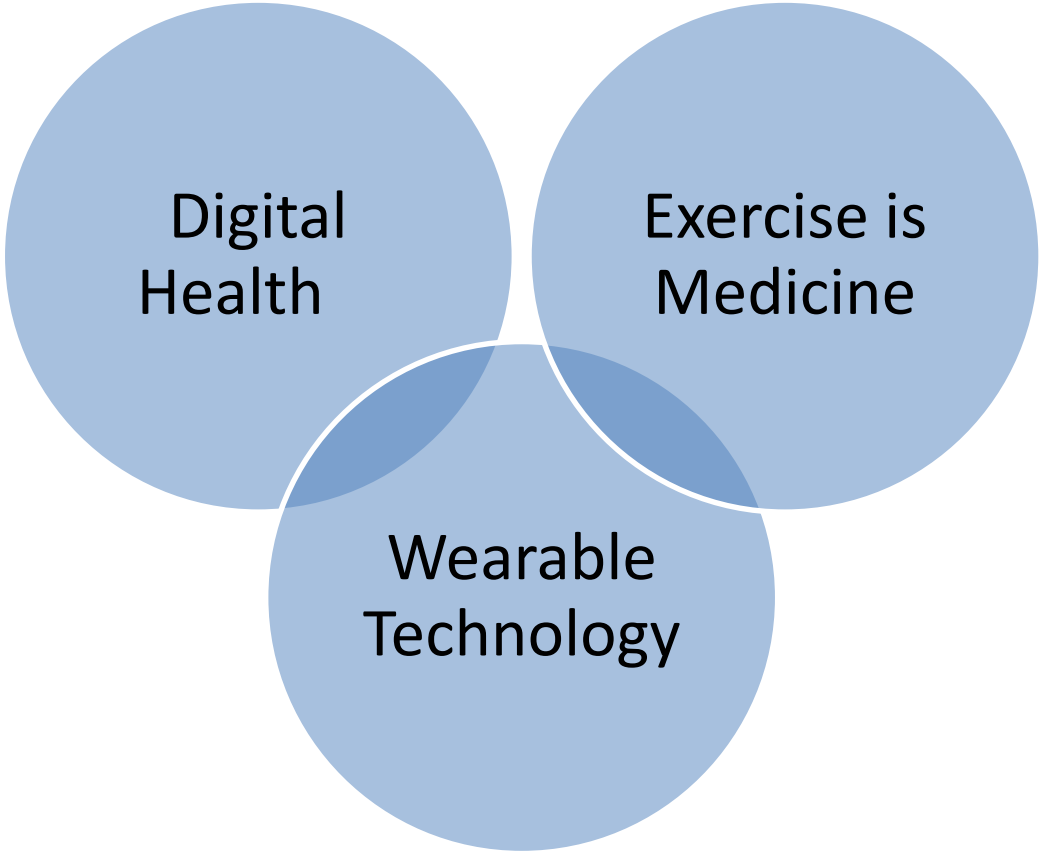
This is Modern Medicine



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Digital Health

Prof David Burke

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CAPTION Health

- Performing cardiac echocardiography is a difficult process and requires significant training and expertise
- Caption Health has developed an innovative AI guidance system using deep learning algorithms, that allows novice users to obtain echo images
- FDA approved in 2020
- Aim to provide ‘point of care’ U/S and to free up the ‘bottle neck’ in demand for scanning

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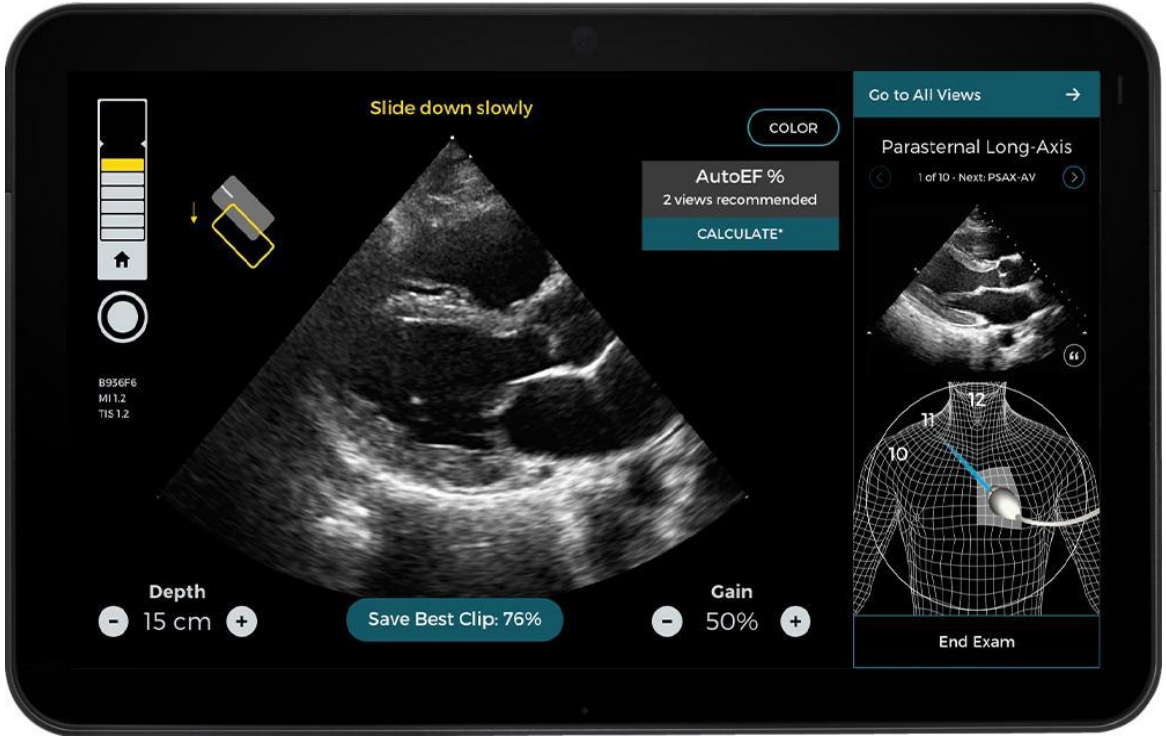
Expert Guidance



Caption AI emulates the expertise of a sonographer by providing **real-time guidance** that prompts users to make specific transducer movements to optimize and capture a diagnostic-quality image.

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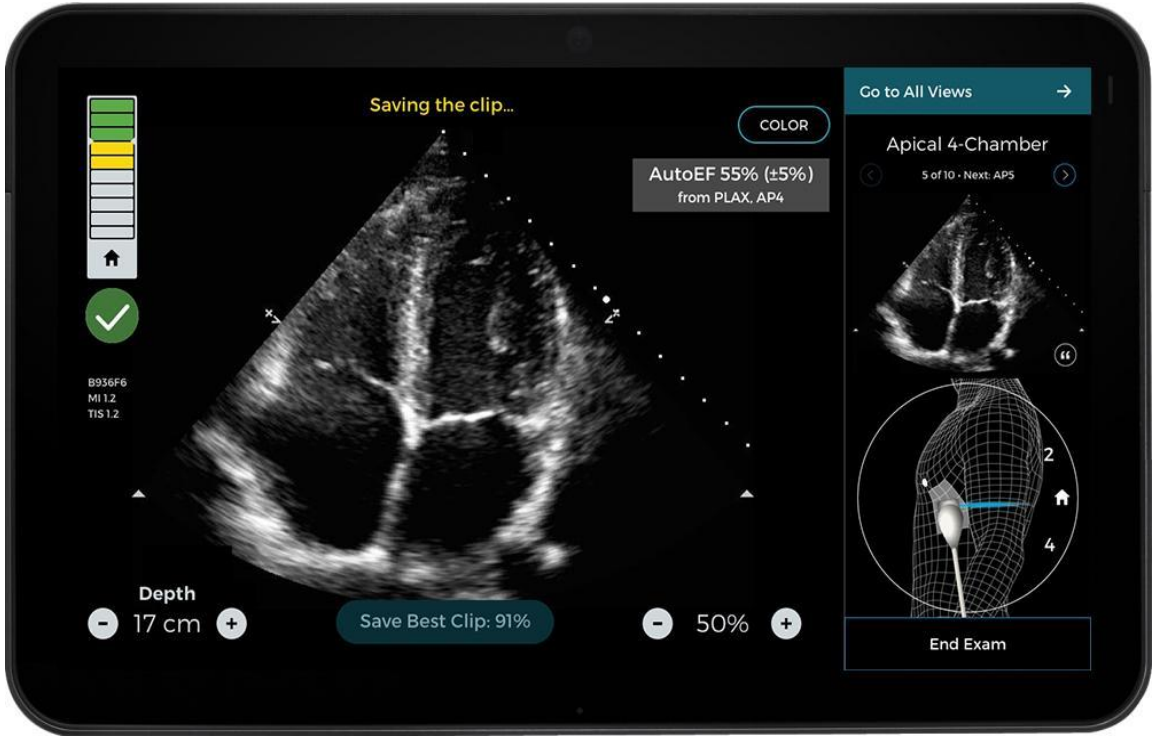
Automated Quality Assessment & Interpretation



Caption AI helps standardize and ensure diagnostic-quality exams.

The **Quality Meter** shows users in real time how close they are to capturing a diagnostic-quality image.

AutoCapture records the clip, hands-free.

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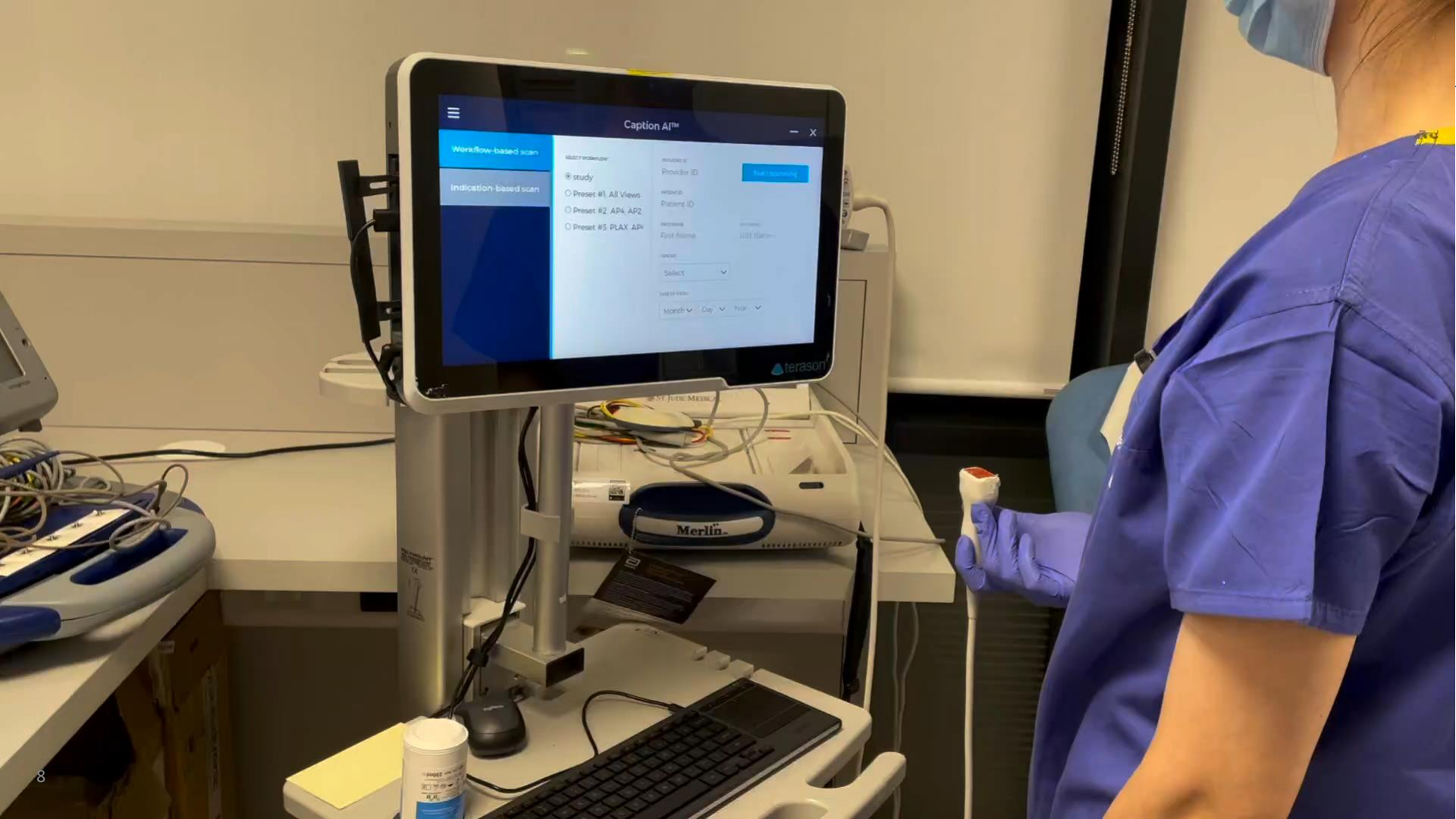
Caption AI™
Workflow-based scan
Indication-based scan
study
Preset #1. All Views
Preset #2. AP4, AP2
Preset #3. PLAX, AP4
Provider ID
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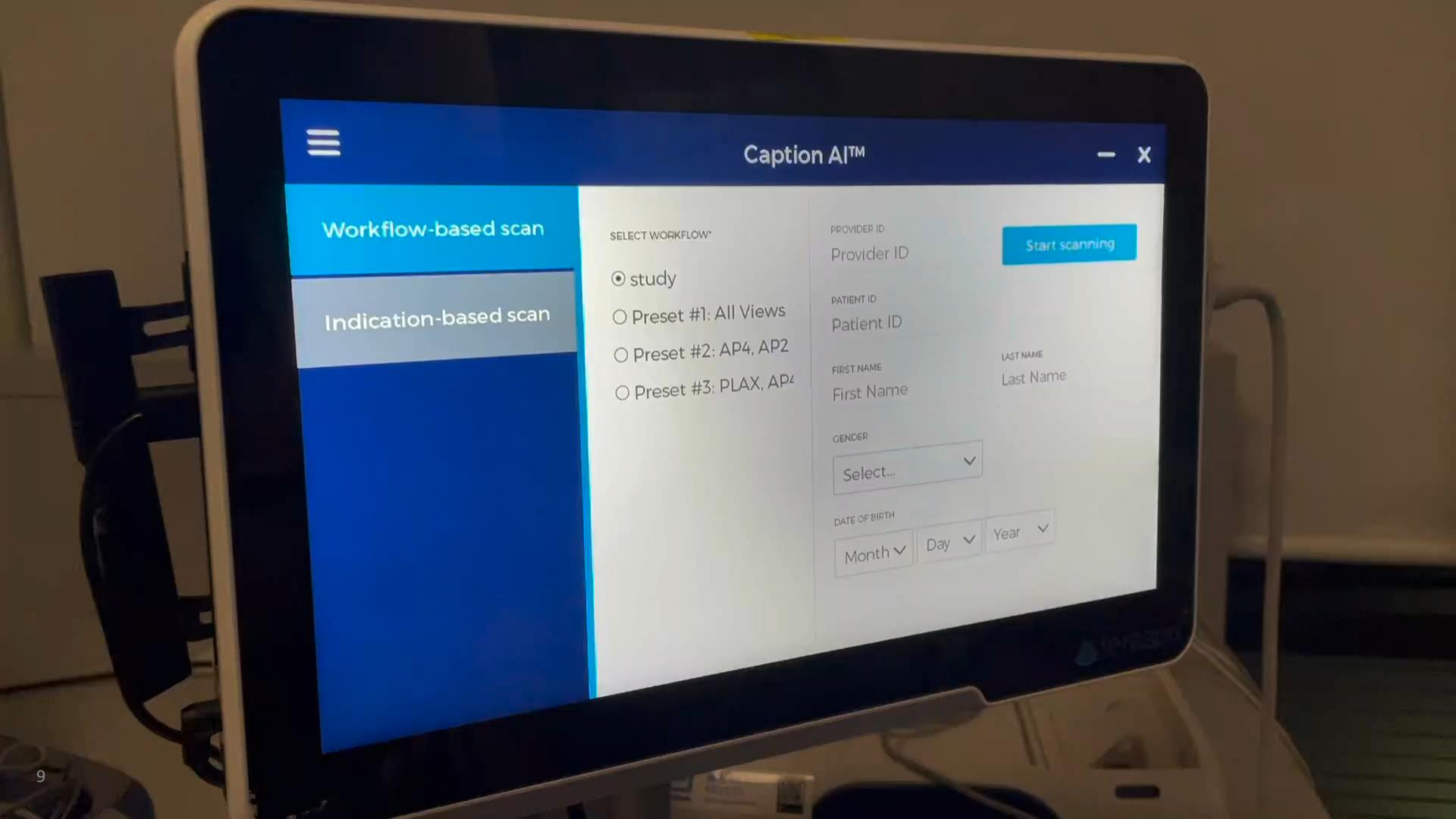
Caption AI™
Workflow-based scan
Indication-based scan
SELECT WORKFLOW*
study
Preset #1: All Views
Preset #2: AP4, AP2
Preset #3: PLAX, AP
PROVIDER ID
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PATIENT ID
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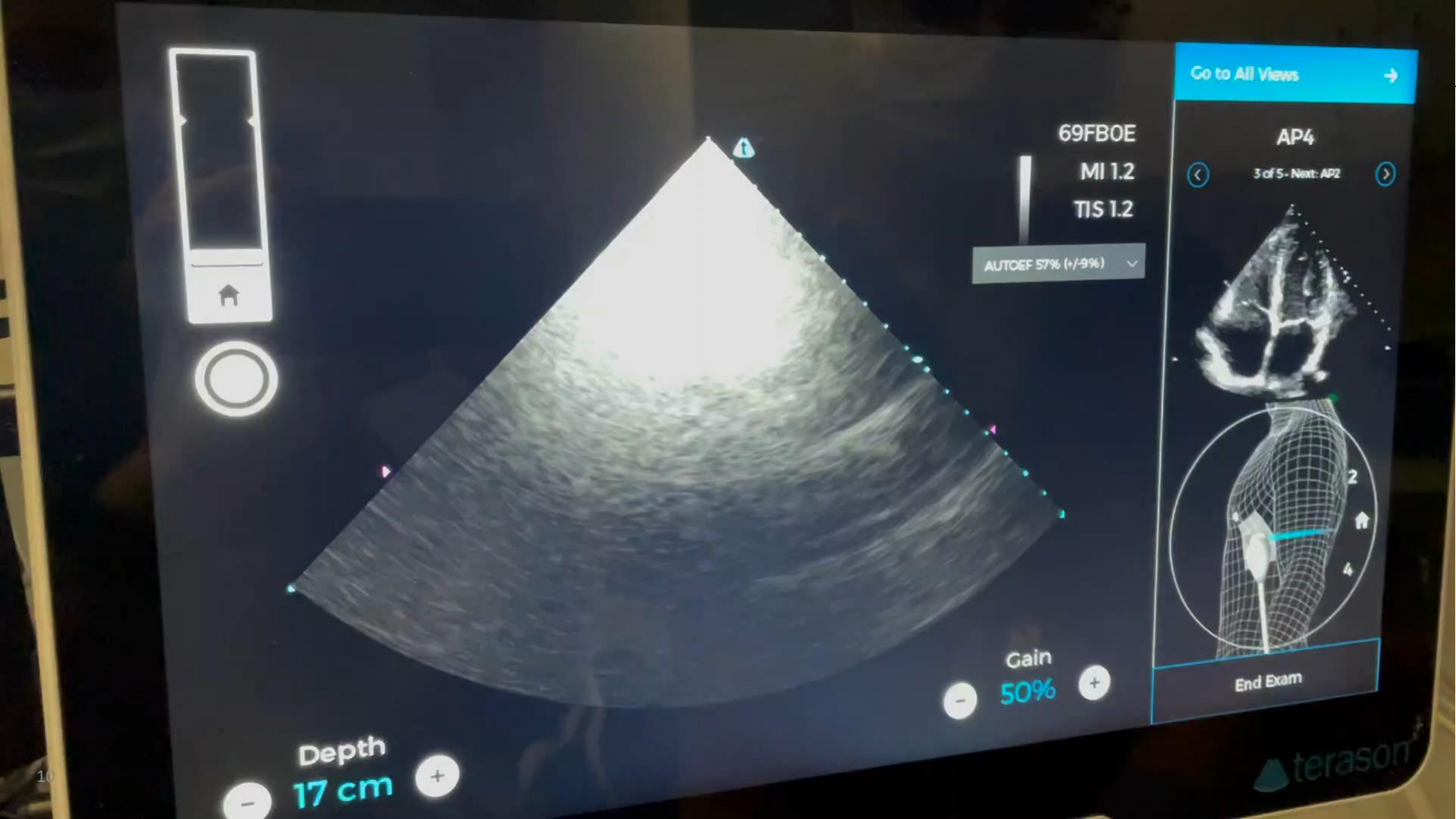
First Name
LAST NAME
Last Name
GENDER
Select...
DATE OF BIRTH
Month
Day
Year


69FB0E
MI 1.2
TIS 1.2
AUTOEF 57% (+/-9%)
Go to All Views
AP4
3 of 5 - Next: AP2
2
4
End Exam
Gain
50%
Depth
17 cm
terason

First European Study at Beacon

- Enrolled 120 patients – 30 in each of ED, ICU, HF clinic, Onc Day Ward
- 2 'novice' scanners in each clinical area
- Study matched with 'expert' scan
- Independently reviewed and analysed

- Demographics – age range 18 – 92yo 75% male. BMI 18 – 37.5
- Sufficient imaging to determine LV function, RV and pericardial effusion in >97.5%
- AutoEF in 88% - close correlation with expert
- 'Novice' scan equal or better in quality in 60% cases

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Real world evaluation of artificial intelligence echocardiography image guidance and acquisition with novice scanners in multiple clinical settings.

DA. Burke[1], N. Corrigan[1], M. Herlihy[1], O. Nasaj[1], J. Dickson[1], D. Delaney[1], J. Westrup[2] - (1) Beacon Hospital, Cardiology Department, Dublin, Ireland (2) Beacon Hospital, Dublin, Ireland

BACKGROUND:

- Cardiac echocardiographic scanning requires significant training and experience.
- The FDA approved Caption Echocardiography system uses a deep learning artificial intelligence software that guides novice scanners to optimal position and then automatically acquires the highest quality image. (Figures 1 and 2).
- Further advances to this novel technology have allowed for immediate calculation of left ventricular ejection fraction directly from these images. (Figure 3).

METHODS:

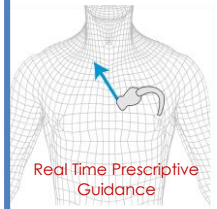
- Following only brief training, we sought to evaluate study quality by novice scanners in four clinical settings, both acute and ambulatory – the Emergency Department, Intensive Care Unit, Heart Failure clinic, and the Oncology Day Unit.
- 120 patients (30 per clinical area) were recruited and underwent 2 echo scans – one by a novice scanner using the Caption AI system, and one by an expert scanner using the same ultrasound system but without AI guidance.
- Both studies were evaluated blindly and independently side by side by 3 accredited experts judging diagnostic quality.
- 'AutoEF' measurements were compared with expert scanners measurements by Simpson's biplane technique.

RESULTS:

- Of 120 patients across 4 service areas, age 18-92 yo (mean 62.04), 75% male, BMI range 18.03 – 37.55 (mean 27.48).
- Image quality was sufficient to determine LV function 97.5% (117/120) of time, RV function 95% (114/120), and out rule pericardial effusion 97.5% (117/120).
- The software was able to calculate 'AutoEF' in 88.3% of patients (106/120) and was accurate compared with expert 84% of the time. The remaining 16% of EF measurements were underestimated, with no overestimates. (See table 1).

Table 1: AutoEF calculation vs 'expert' measurement

AUTO EF	ED	HF CLINIC	ICU	ONC DAY	OVERALL
Auto EF Available (%)	90 (27/30)	93.3 (28/30)	90 (27/30)	80 (24/30)	88.3 (106/120)
Equal with Expert (%)	77.8 (21/27)	85.7 (24/28)	92.6 (25/27)	79.2 (19/24)	84 (89/106)
Underestimated (%)	22.2 (6/27)	14.3 (4/28)	7.4 (2/27)	20.8 (5/24)	16 (17/106)



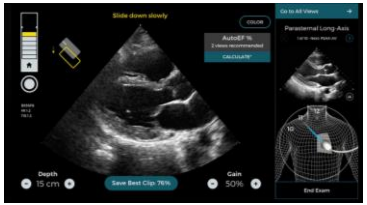


Fig 1. User interface showing real time guidance to reach optimal position and automatically acquire image

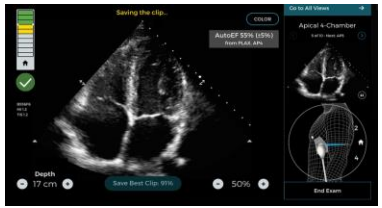


Fig 2. Autocapture records best diagnostic image when quality meter reaches threshold, before moving to next image angle

Fig 3. 'AutoEF' is calculated automatically from the captured apical-4-chamber, AP2, and parasternal long axis loops.

CONCLUSION:

- The Caption AI technology safely allows novice users to provide efficient and accurate point of care echo in differing clinical settings to a standard comparable to expert scanners, and automatically determines left ventricular ejection fraction with a high degree of accuracy.

Wearable Technology

Prof David Burke

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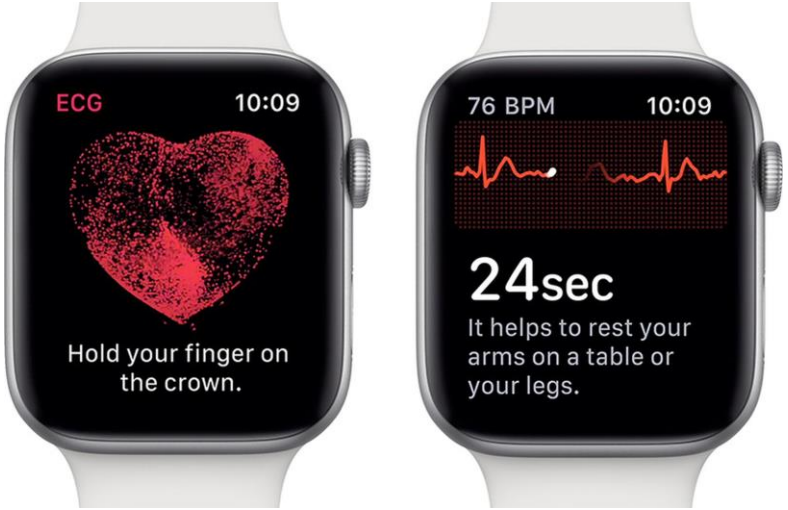
Ongoing Projects

- Heart failure management
    - Fitbit continuous monitoring and Bluetooth connected weighing scales
- Covid detection – DETECT 2 study
- Cardiac Rehabilitation – in person and virtual
- Galenband – EI comm fund. Bioinnovate spin out. Atrial fibrillation detection

Potential & Future Utility

- Continuous heart monitoring
- Dynamic management of chronic conditions
- Arrhythmia detection



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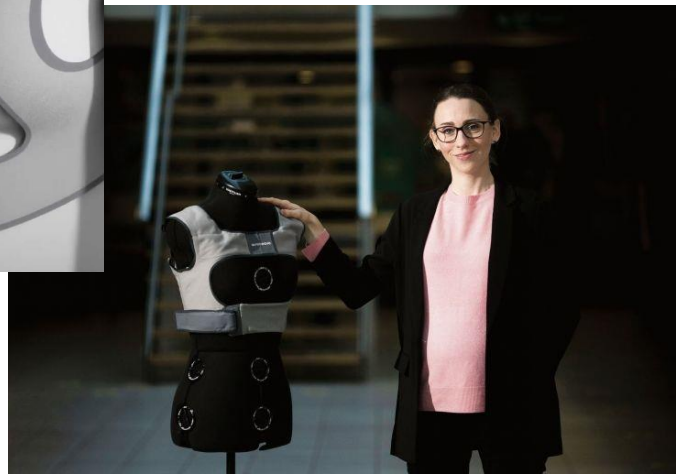
ResWave project

- ResWave have developed a device designed to reduce the sense of dyspnoea in COPD patients
- Wearable, non-invasive device using neuromuscular stimulation assist in the relief of breathlessness
- Starting with a pilot study of feasibility for the use of the vest



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Why is this Important?

- Vicious cycle of inactivity with progression of COPD
- Adjuncts to help relieve breathlessness are limited
- Evidence around neuromuscular stimulation and relief of breathlessness exists, but no practical applications available to date

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ResWave Project

- Light weight and discreet
- Durable and can be worn under clothing
- The mechanism:
  - The device modulates afferent neurological impulses from the respiratory muscles and airways, altering respiratory sensations perceived by the brain
  - This helps to compensate for the altered respiratory muscle mechanics that can occur in COPD

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Beacon Hospital Research Proposal

Design:
This will be a randomised controlled study with sham control.
20 participants will undergo structured exercise testing (CPET) with and without the device.

Objectives
The study aims to:
Evaluate prototype device design with respect to:

- Clinical safety and side effect profile (Primary Outcome)
- Gather preliminary efficacy data (Secondary Outcomes) (data from CPET & patient perceived exertion)

Provide initial validation and data to guide design of a larger subsequent studies
Provide performance data to guide future prototype development

Population:
Adults with diagnosis of COPD and FEV1 of 35 - 75% predicted who are suitable for participating in Cardiopulmonary Exercise Testing.

Primary outcomes: adverse events, device deficiencies
Secondary outcomes: validated dyspnoea scores during exertion, Exercise Endurance Time

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Summary

- Is a wearable, non-invasive device using neuromuscular stimulation feasible and safe?

- Can it assist in the relief of breathlessness in COPD?

If effective...

- Primarily intended to assist with exertional dyspnoea that occurs with activities of daily living
- Assist users with maintaining their functional status and breaking the 'vicious cycle' of increasingly sedentary behaviour.
- It is anticipated that it will be an adjust to establish drug therapies.

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Exercise is Medicine

Ailish Daly

Beacon Hospital
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Research Proposal

- Research question?
  - Does exercise before or during chemotherapy infusion improve patient outcomes.

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Beacon Hospital Research Proposal:

Inclusion criteria

- 18 years and over
- Newly diagnosed breast cancer patients starting first line AC-T chemotherapy
- ECOG score 0-1 (Eastern Co-operative Oncology Group)
- Able to read, write and understand English
- Able to engage in 20-30 minutes physical activity
- BMI less than 30
- Able to independently mount, dismount and use exercise bike

Screening

- Screened by Consultant Oncologist and Informed about the study

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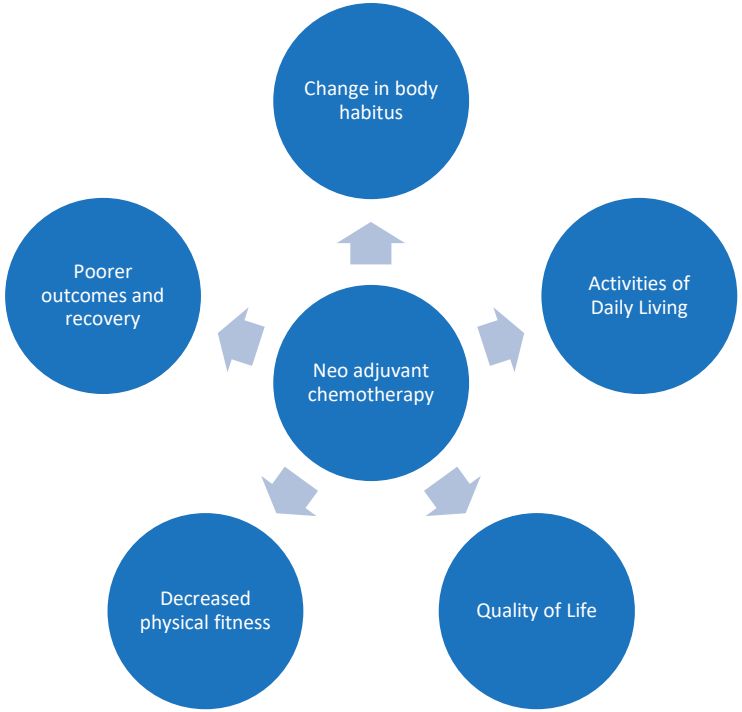
Why is this Study Important?



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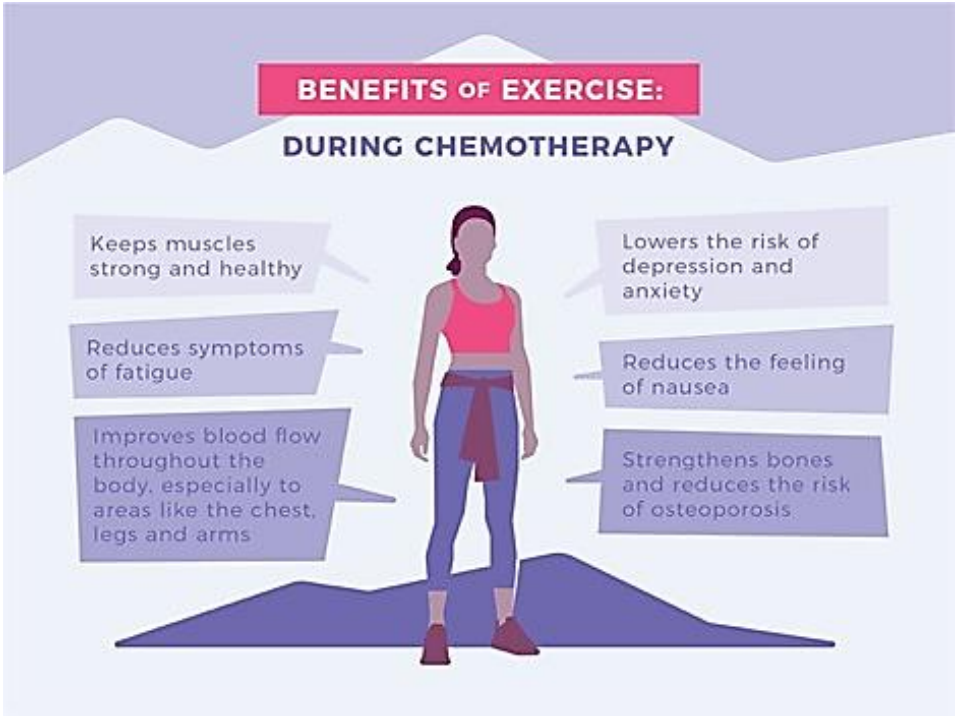
Impact of Exercise During Chemotherapy



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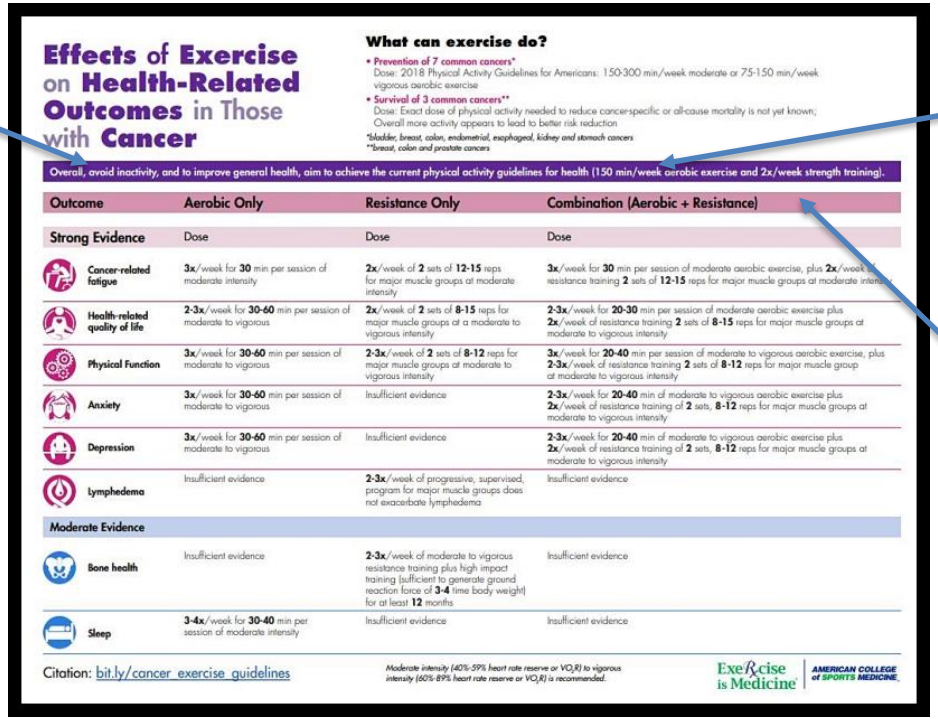
ACSEM Guidelines

Avoid inactivity

150 min / week aerobic exercise

X 2 / week strength training



Effects of Exercise on Health-Related Outcomes in Those with Cancer

What can exercise do?

- **Prevention of 7 common cancers***
  Dose: 2018 Physical Activity Guidelines for Americans: 150-300 min/week moderate or 75-150 min/week vigorous aerobic exercise
- **Survival of 3 common cancers****
  Dose: Exact dose of physical activity needed to reduce cancer-specific or all-cause mortality is not yet known; Overall more activity appears to lead to better risk reduction

*bladder, breast, colon, endometrial, esophageal, kidney and stomach cancers
**breast, colon and prostate cancers

Overall, avoid inactivity, and to improve general health, aim to achieve the current physical activity guidelines for health (150 min/week aerobic exercise and 2x/week strength training).

Outcome	Aerobic Only	Resistance Only	Combination (Aerobic + Resistance)
Strong Evidence	Dose	Dose	Dose
Cancer-related fatigue	**3x**/week for **30** min per session of moderate intensity	**2x**/week of **2** sets of **12-15** reps for major muscle groups at moderate intensity	**3x**/week for **30** min per session of moderate aerobic exercise, plus **2x**/week of resistance training **2** sets of **12-15** reps for major muscle groups at moderate intensity
Health-related quality of life	**2-3x**/week for **30-60** min per session of moderate to vigorous	**2x**/week of **2** sets of **8-15** reps for major muscle groups at a moderate to vigorous intensity	**2-3x**/week for **20-30** min per session of moderate aerobic exercise plus **2x**/week of resistance training **2** sets of **8-15** reps for major muscle groups at moderate to vigorous intensity
Physical Function	**3x**/week for **30-60** min per session of moderate to vigorous	**2-3x**/week of **2** sets of **8-12** reps for major muscle groups at moderate to vigorous intensity	**3x**/week for **20-40** min per session of moderate to vigorous aerobic exercise, plus **2-3x**/week of resistance training **2** sets of **8-12** reps for major muscle group at moderate to vigorous intensity
Anxiety	**3x**/week for **30-60** min per session of moderate to vigorous	Insufficient evidence	**2-3x**/week for **20-40** min of moderate to vigorous aerobic exercise plus **2x**/week of resistance training of **2** sets, **8-12** reps for major muscle groups at moderate to vigorous intensity
Depression	**3x**/week for **30-60** min per session of moderate to vigorous	Insufficient evidence	**2-3x**/week for **20-40** min of moderate to vigorous aerobic exercise plus **2x**/week of resistance training of **2** sets, **8-12** reps for major muscle groups at moderate to vigorous intensity
Lymphedema	Insufficient evidence	**2-3x**/week of progressive, supervised, program for major muscle groups does not exacerbate lymphedema	Insufficient evidence
Moderate Evidence			
Bone health	Insufficient evidence	**2-3x**/week of moderate to vigorous resistance training plus high impact training (sufficient to generate ground reaction force of **3-4** time body weight) for at least **12** months	Insufficient evidence
Sleep	**3-4x**/week for **30-40** min per session of moderate intensity	Insufficient evidence	Insufficient evidence

Citation: bit.ly/cancer_exercise_guidelines

Moderate intensity (40%-59% heart rate reserve or VO_2R) to vigorous intensity (60%-89% heart rate reserve or VO_2R) is recommended.

Exercise is Medicine | AMERICAN COLLEGE of SPORTS MEDICINE

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What is Next?

- Animal studies
- Exercise can change tumour microenvironment
- Remodel tumour vasculature
- Can this improve perfusion to tumour?
- Can this improve chemotherapy penetration?

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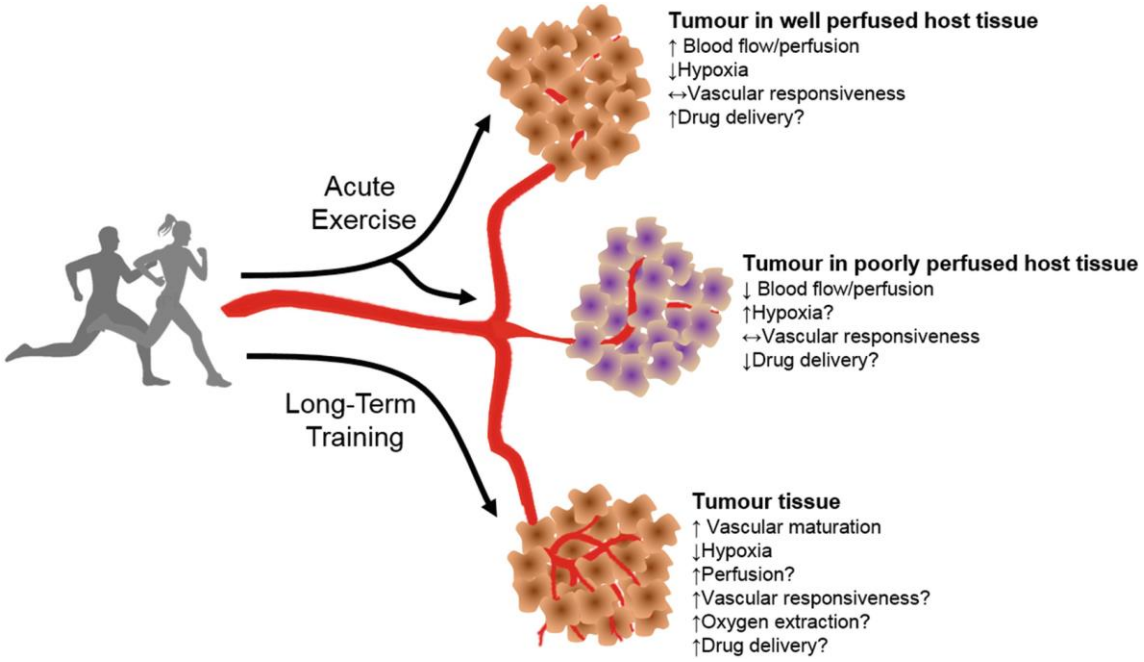
What If?



- Improve vasodilation and perfusion to the tumour
- Improve chemotherapy penetration
- Improve tumour regression

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What We Know So Far (Safety And Feasibility Study)

Thomas, V., Seet-Lee, C., Marthick, M et al (2020) Aerobic exercise during chemotherapy infusion for cancer treatment: a novel randomised crossover safety and feasibility trial. Supportive Care in Cancer. Volume 28

Study question:
Is it safe and feasible to perform aerobic exercise during chemotherapy infusion for cancer treatment?
Adults undergoing chemotherapy

- Exercises for 20 minutes low intensity cycling
- 2 consecutive chemotherapy infusions

Outcomes

- Safety : It is safe to exercise during chemotherapy infusion
- Opportunities: Exercise significantly reduce boredom during infusion
- No significant different in symptoms experienced
- No significant difference in difficulty or comfort levels
- 65% of eligible patients agreed

Next steps:

- drug delivery efficiency
- symptom reduction
- opportunity for physical activity increase

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What We Know (Case Study)

McLaughlin, M;, Christie, A., Campbell, A (2019) Case Report of Exercise to Attenuate Side Effects of Treatment for Pancreatic Cancer. Case reports in Oncology 12 (3)

Study question:

Does exercise during chemotherapy infusion attenuate the side effects of treatment for Pancreatic Cancer?

- 47 year old male
- Chemotherapy for stage 3 locally advanced pancreatic cancer
- Cycled during hospital chemotherapy infusions (6 fortnightly cycles of Folfirinox)
- 12 weeks twice weekly aerobic and resistance exercise

Outcomes

- Over 12 weeks
- Maintained body composition
- Physical function improved
- Muscle strength increased by 50%
- Aerobic capacity improved by 9%
- QOL improved by 38%
- Psychological distress improved by 50%
- Sleep quality improved by 9%

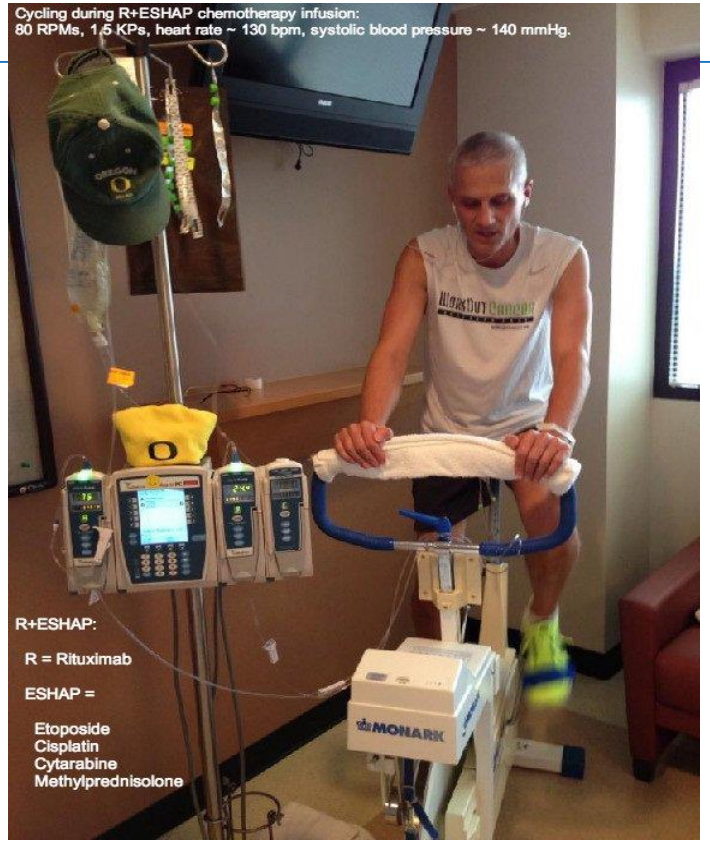
Conclusion: Exercise reduced side effects of treatment for pancreatic cancer

Summary

Does exercise pre and during infusion improve outcomes?

Study endpoint: On completion of chemotherapy

- Tumour size
- Changes in ctDNA
- Patient feedback/satisfaction
- Reduction in side effects and dose reductions
- Cardiopulmonary fitness (CPET)
- Quality of life (EORTC QLQ C30)



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Summary: ACSEM Guidelines

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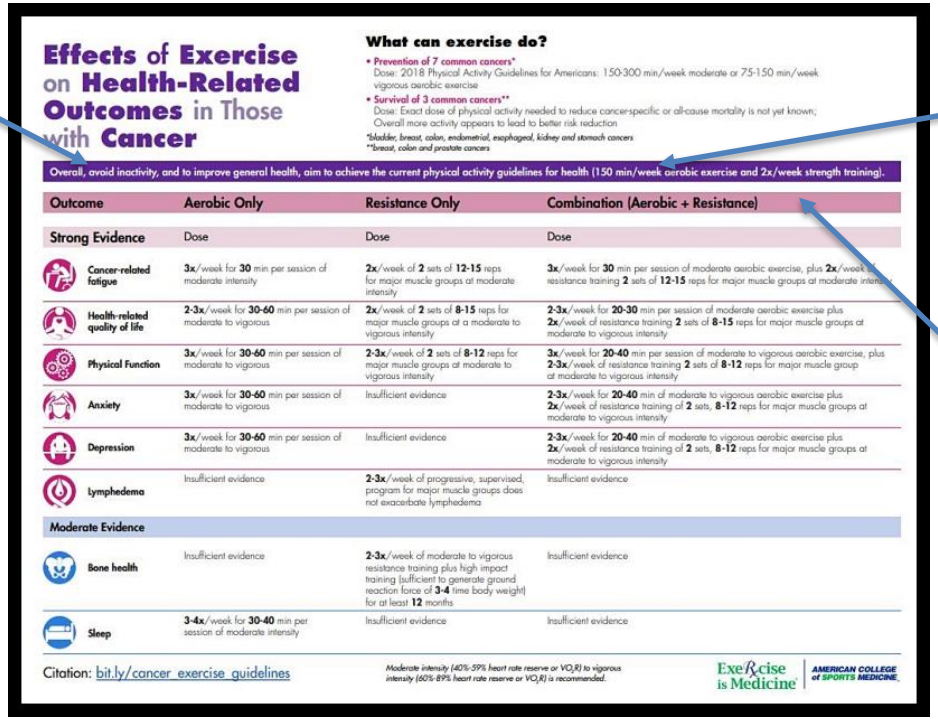

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What This Will Mean For Our Patients

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Cancer Services

Fit for Life Programme

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Beacon Hospital Research Institute

Research Ethics Committee

Clinical Audit Committee

Supportive Capacity

1. Institute manager
2. Data Analyst
3. PSQI member

Research Associates / Research Nurses

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Ongoing Studies: Orthopaedics

Insight
SFI RESEARCH CENTRE FOR DATA ANALYTICS

NOVARTIS

Validating Sensor Technology in OA

- Validation of a new approach to measure dynamic knee loading in healthy volunteers and osteoarthritis (OA) patients

KNiT
Knee Injection Therapy Trial

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Knee Osteoarthritis Injection Therapy (KNiT) Trial

- Interventional, randomised, injection protocols in Knee OA

Ongoing studies: Radiotherapy

- DASL- HiCaP

- A randomized phase 3 trial of adding darolutamide to radiation and androgen deprivation therapy in high risk, clinically localized prostate cancer.

- IRONMAN

- International Registry for Men with Advanced Prostate Cancer

Ongoing Studies: Anaesthesia and Critical Care Medicine

Short PeRiod IncideNce sTudy of Severe Acute Respiratory Infection

SPRINT SARI

- International multi centre observational study of participants with severe acute respiratory infection

Randomised, Embedded, Multi-factorial, Adaptive Platform Trial for Community-Acquired Pneumonia

REMAP-CAP

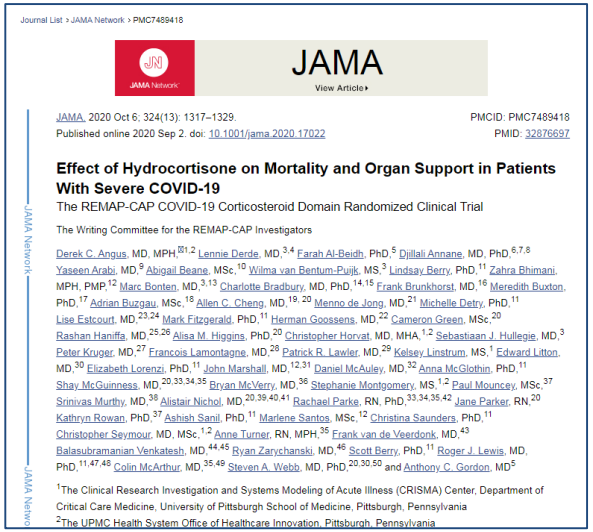
- Multiple domains for CAP and COVID patients in ICU – 14 domains across trial
- Multiple reports globally examining characteristics in COVID 19

Trial of Early Activity and Mobilisation

TEAM ICU

- International trial on early mobility in invasively mechanically ventilated patients in ICU
- Physiotherapy based trial/Interdepartmental cross collaboration

BHRI Dissemination and Visibility



Journal List › JAMA Network › PMC7489418

JAMA

View Article ▸

JAMA. 2020 Oct 6; 324(13): 1317–1329. PMCID: PMC7489418
Published online 2020 Sep 2. doi: 10.1001/jama.2020.17022 PMID: 32876697

Effect of Hydrocortisone on Mortality and Organ Support in Patients With Severe COVID-19

The REMAP-CAP COVID-19 Corticosteroid Domain Randomized Clinical Trial

The Writing Committee for the REMAP-CAP Investigators

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ORIGINAL ARTICLE

Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19

The REMAP-CAP Investigators*

Article Figures/Media Metrics

26 References 186 Citing Articles Letters 2 Comments

April 22, 2021
N Engl J Med 2021; 384:1491-1502
DOI: 10.1056/NEJMoa2100433

Abstract

BACKGROUND

The efficacy of interleukin-6 receptor antagonists in critically ill patients with coronavirus disease 2019 (Covid-19) is unclear.

METHODS

We evaluated tocilizumab and sarilumab in an ongoing international, multifactorial, adaptive platform trial. Adult patients with Covid-19, within 24 hours after starting organ support in the intensive care unit (ICU), were randomly assigned to receive tocilizumab (8 mg per kilogram of body weight), sarilumab (400 mg), or standard care (control). The primary outcome was respiratory and cardiovascular organ support–free days, on an ordinal scale combining in-hospital death (assigned a value of -1) and days free of organ support to day 21. The trial uses a Bayesian statistical model with predefined criteria for superiority, efficacy, equivalence, or futility. An odds ratio greater than 1 represented improved survival,

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ORIGINAL ARTICLE APR 22, 2021
Tocilizumab in Hospitalized Patients w
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CORRESPONDENCE AUG 18, 2021
Interleukin-6 Receptor Antagonists in
Patients with Covid-19

Intensive Care Med (2021) 47:867–886
https://doi.org/10.1007/s00134-021-06448-5

ORIGINAL

Lopinavir-ritonavir and hydroxychloroquine for critically ill patients with COVID-19: REMAP-CAP randomized controlled trial

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Abstract

Purpose: To study the efficacy of lopinavir-ritonavir and hydroxychloroquine in critically ill patients with coronavirus disease 2019 (COVID-19).

Methods: Critically ill adults with COVID-19 were randomized to receive lopinavir-ritonavir, hydroxychloroquine, combination therapy of lopinavir-ritonavir and hydroxychloroquine or no antiviral therapy (control). The primary endpoint was an ordinal scale of organ support-free days. Analyses used a Bayesian cumulative logistic model and expressed treatment effects as an adjusted odds ratio (OR) where an OR > 1 is favorable.

Results: We randomized 694 patients to receive lopinavir-ritonavir ($n = 255$), hydroxychloroquine ($n = 50$), combina-

Therapeutic Anticoagulation with Heparin in Critically Ill Patients with Covid-19

The REMAP-CAP, ACTIV-4a, and ATTACC Investigators*

Article Figures/Media Metrics

27 References 2 Citing Articles

August 26, 2021
N Engl J Med 2021; 385:777-789
DOI: 10.1056/NEJMoa2103417

Abstract

BACKGROUND

Thrombosis and inflammation may contribute to morbidity and mortality among patients with coronavirus disease 2019 (Covid-19). We hypothesized that therapeutic-dose anticoagulation would improve outcomes in critically ill patients with Covid-19.

METHODS

In an open-label, adaptive, multiplatform, randomized clinical trial, critically ill patients with severe Covid-19 were randomly assigned to a pragmatically defined regimen of either therapeutic-dose anticoagulation with heparin or pharmacologic thromboprophylaxis in accordance with local usual care. The primary outcome was organ support–free days, evaluated on an ordinal scale that combined in-hospital death (assigned a value of -1) and the number of days free of cardiovascular or respiratory organ support up to day 21 among patients who survived to hospital discharge.

RESULTS

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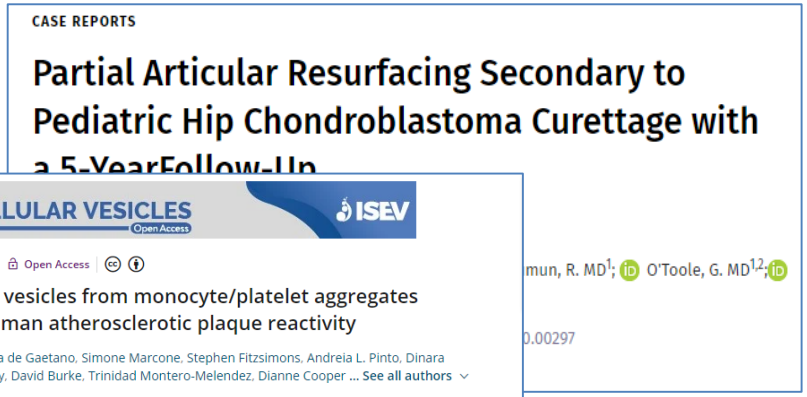

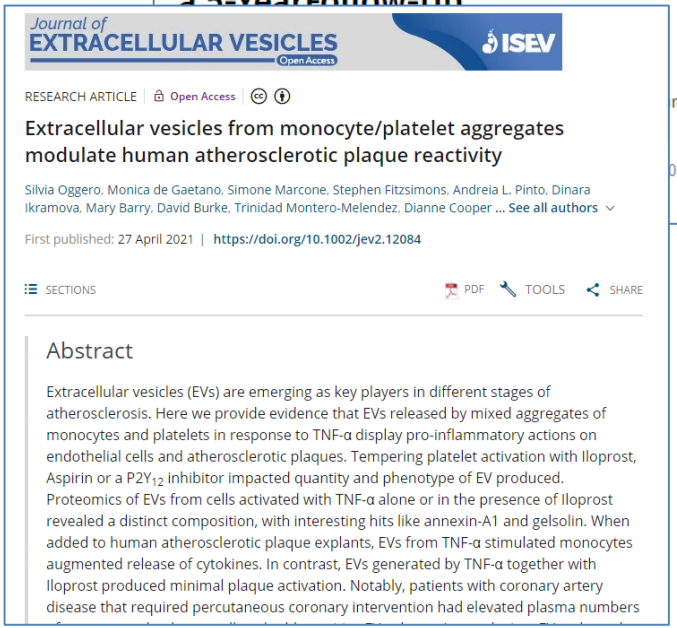

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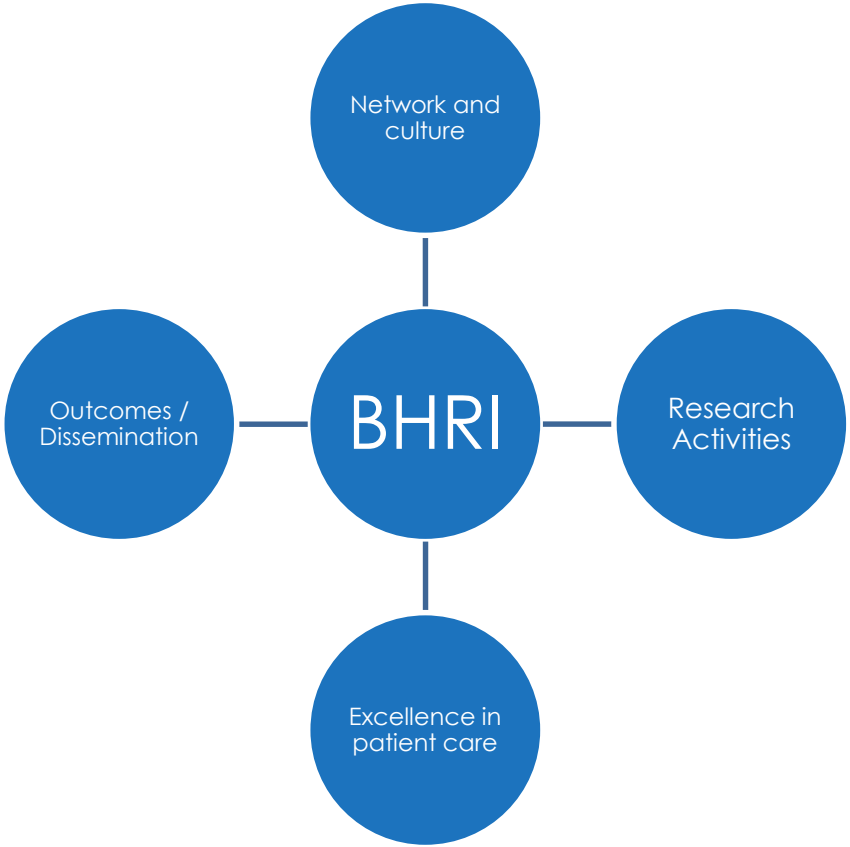

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