CarcinoScope System

Design Review (March 1)

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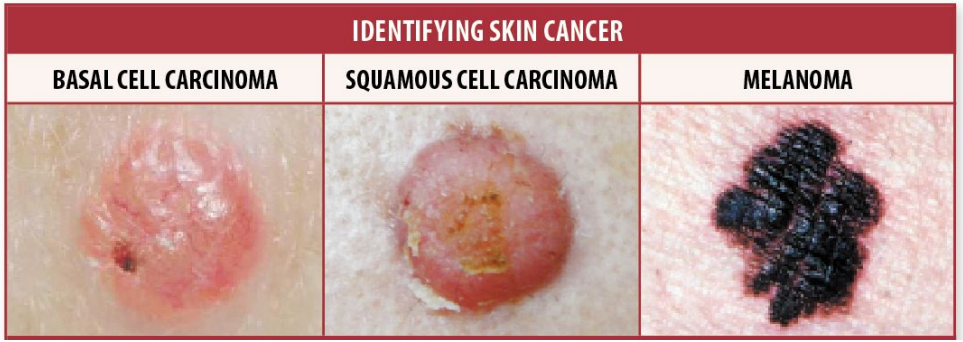
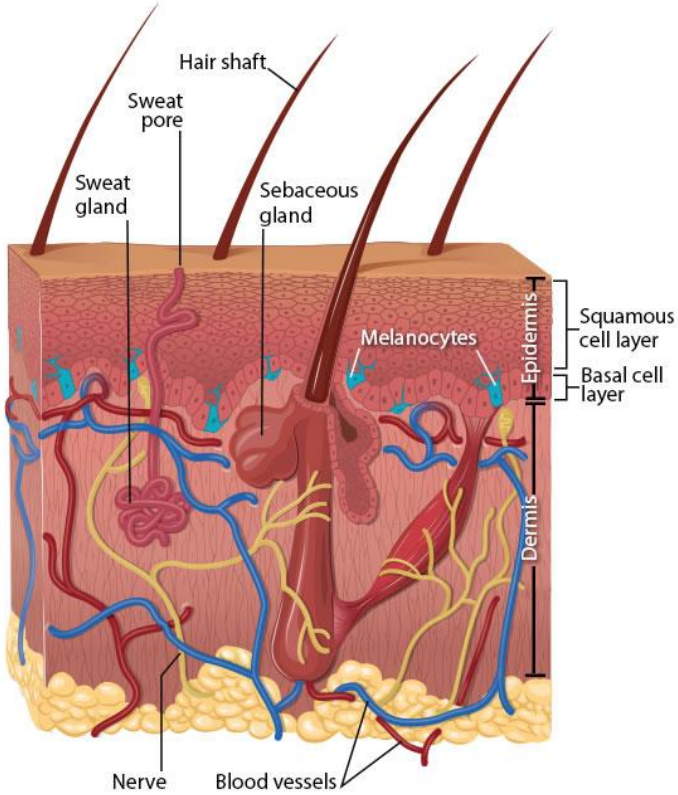
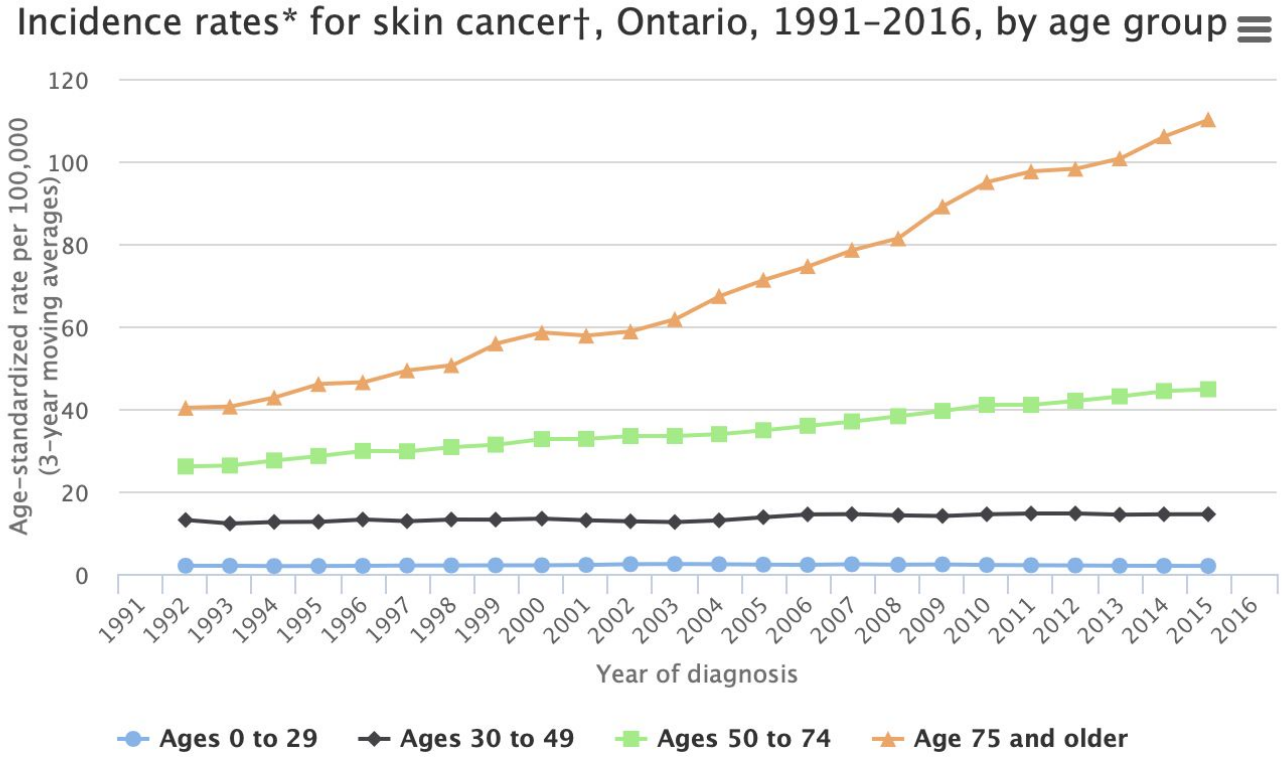
BIOMEDICAL TECHNOLOGIES

Overview: Skin Cancer

- **Non-melanoma skin cancer** (basal cell carcinoma, squamous cell carcinoma) and **melanomas** pathogenesis is considered a multi-hit process involving molecular and genetic changes within melanocytes and skin epithelial cells (de Gruijl & Tensen , 2018)






Incidence rates* for skin cancer†, Ontario, 1991–2016, by age group
Age-standardized rate per 100,000 (3-year moving averages)
120
100
80
60
40
20
0
1991
1992
1993
1994
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
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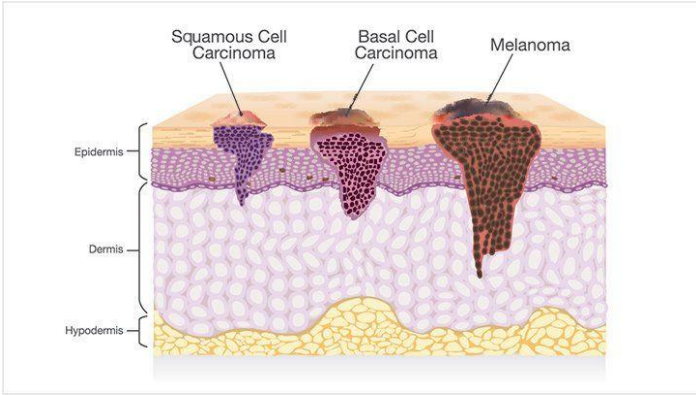
Year of diagnosis
Ages 0 to 29
Ages 30 to 49
Ages 50 to 74
Age 75 and older



Metastasis

Responsible for > 90% of cancer-associated mortality

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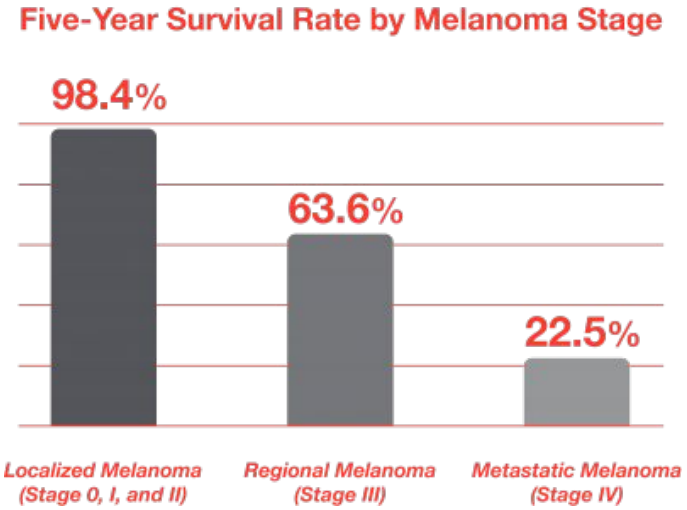
Skin Cancer Incidence & Recurrence Rate

- Over **3.5 million individuals** newly diagnosed with skin cancer in Canada and the United States each year.
    - Over **8,700 Canadians** were diagnosed with melanoma skin cancer in 2021 and **1,250 Canadians** were estimated to die from it (Canadian Cancer Society, 2021)

- NMSC and melanoma have a **5-year recurrence rate of ~10%** necessitating regular medical check-ups and the need to develop fast, effective and time-efficient screening
    - Patients treated for merkel cell cancer have a 5-year recurrence rate of **40%.**



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Limitations in Present Skin Cancer Diagnostics

- **Dermatoscopes** is limited by **low resolution** and **moderate diagnostic sensitivity at 60-80%** depending on the experience of the dermatologist and the lesion being inspected (Wang & Evans, 2016; Papageorgiou et al., 2018)

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Limitations in Present Skin Cancer Diagnostics

- **Reflectance confocal microscopes** are costly, bulky, involving time-consuming setup and small field of view (Levin & Markowitz, 2018)

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CarcinoScope System-MolecuLight i:X

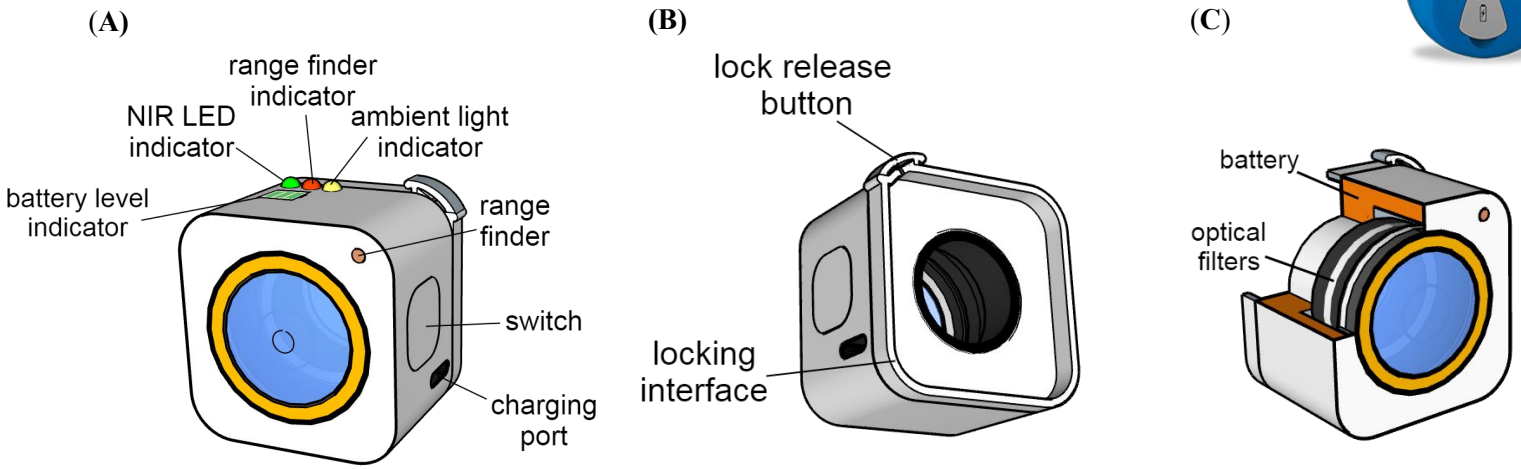

Figure 1. The Carcinoscope System displayed in (**A)** Front, **(B)** Back, and (**C**) Section views.

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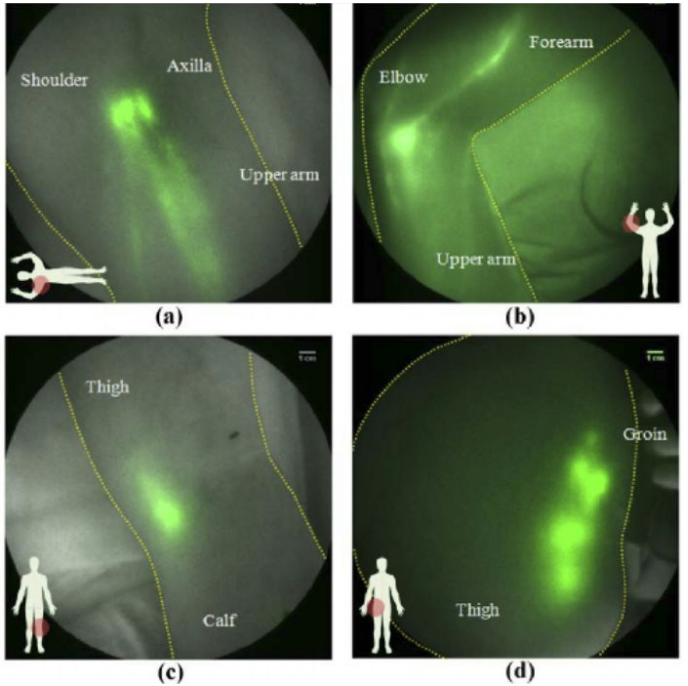
Indocyanine Green (ICG)

- Enables molecular targeting through selective cellular uptake into tumour cells following non-specific administration (topical cream) (Onda et al., 2018)
- Rapidly cleared in normal tissue unlike tumour cells given disruption of their tight junctions and high endocytic activity (Onda et al., 2018)

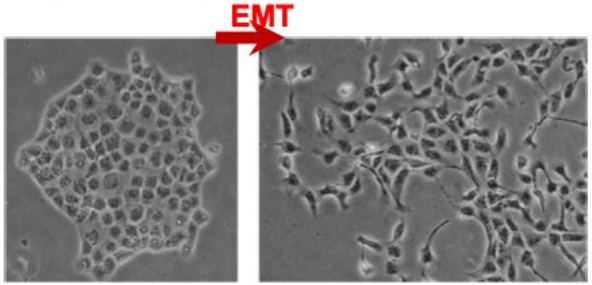


Scientific Principles: Epithelial-to-Mesenchymal Transition

ICG Tumour Localization

Epithelial to Mesenchymal Transition

- Epithelial cell layers in normal tissue: organized, incompatible with motility/invasiveness
- In order to acquire motility: cells undergo a drastic alteration: **EMT**



Characteristics of cells undergoing EMT:

1. Lose cell-cell contacts
2. Acquire mesenchymal morphology (elongated, actin stress fibers)
3. Migratory phenotype
4. Invasive: increase in protease activity e.g., MMPs
5. Proliferative

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ICG Tumour-Localization

Epithelial to Mesenchymal Transition

Molecular Definition/Signature of EMT

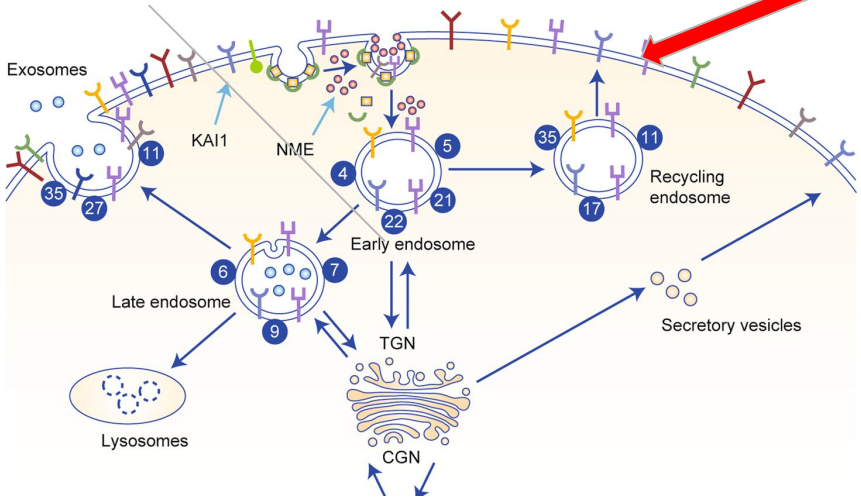
Proteins that decrease in abundance

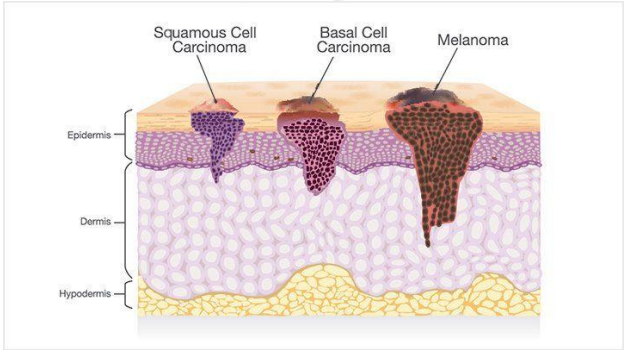
- E-cadherin
- Cytokeratin
- Occludin

Proteins that increase in abundance

- Snail1 (Snail)
- Snail2 (Slug)
- Twist
- Goosecoid
- FOXC2
- Sox10

Transcription factors





(Khan & Steeg, 2020)

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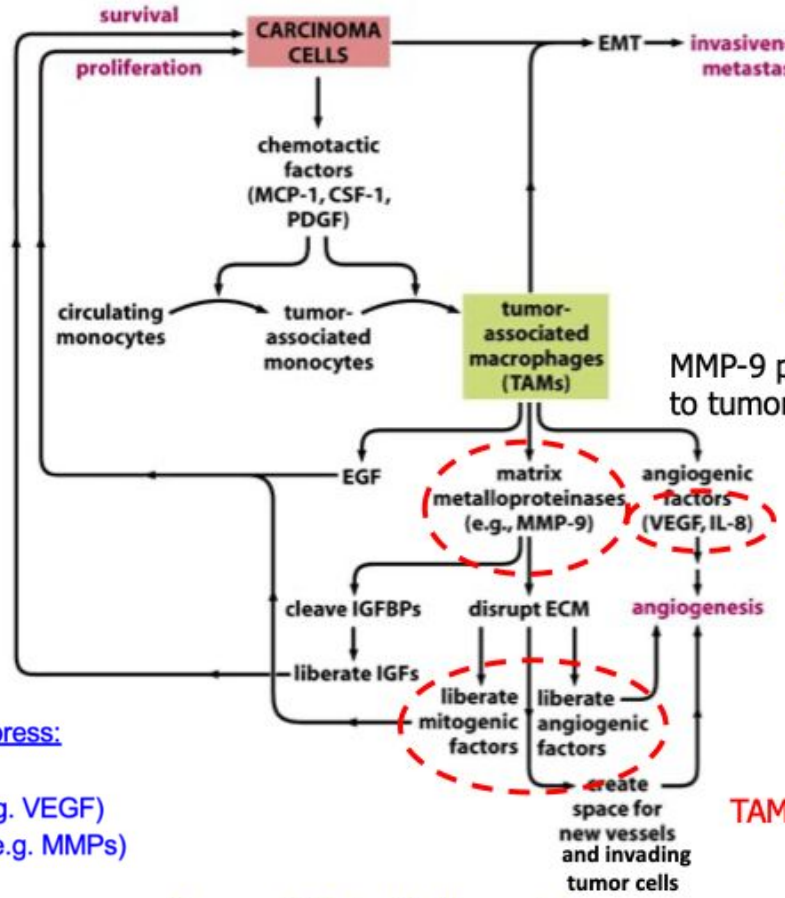
Tumor Microenvironment



Tumor associated macrophages (TAMs) release mitogenic factors for carcinoma cells and reorganize the tumor stroma to facilitate angiogenesis and invasiveness

MMP-9 produced by TAMs contributes to tumor progression:

- enhancing angiogenesis by disrupting existing tissue architecture and providing space to tumor masses to expand
- liberating mitogens from ECM
- cleave IGFBPs, liberating IGF (promotes cancer cell survival)

TAMs: source of EGF, VEGF and IL8

Tumor stromal cells express:

- growth factors
- angiogenic factors (e.g. VEGF)
- proteolytic enzymes (e.g. MMPs)

IGFBP- insulin like growth factor binding protein

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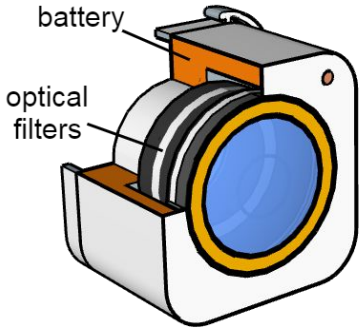
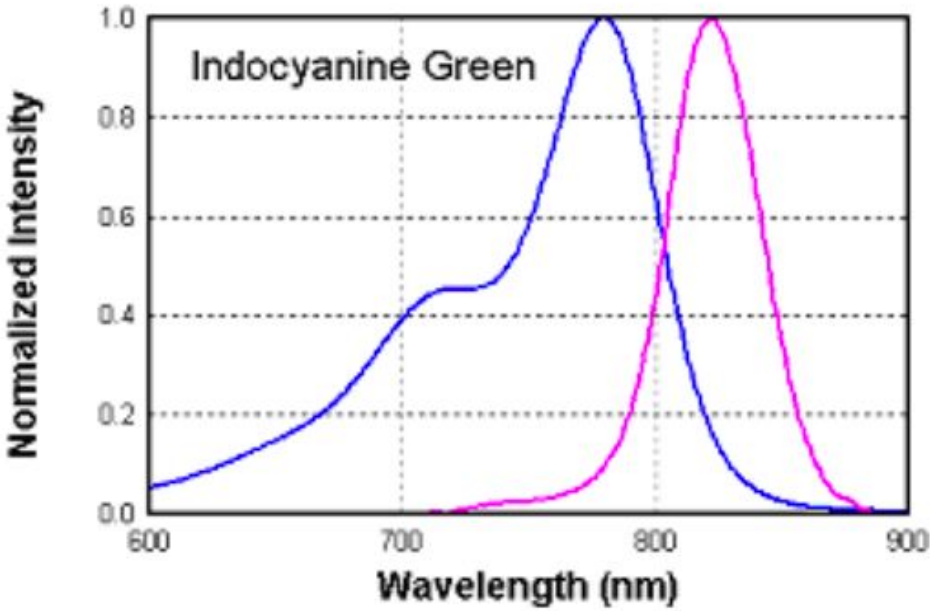
Fluorescence: Technological Components

ICG Fluorescence Detection & Imaging





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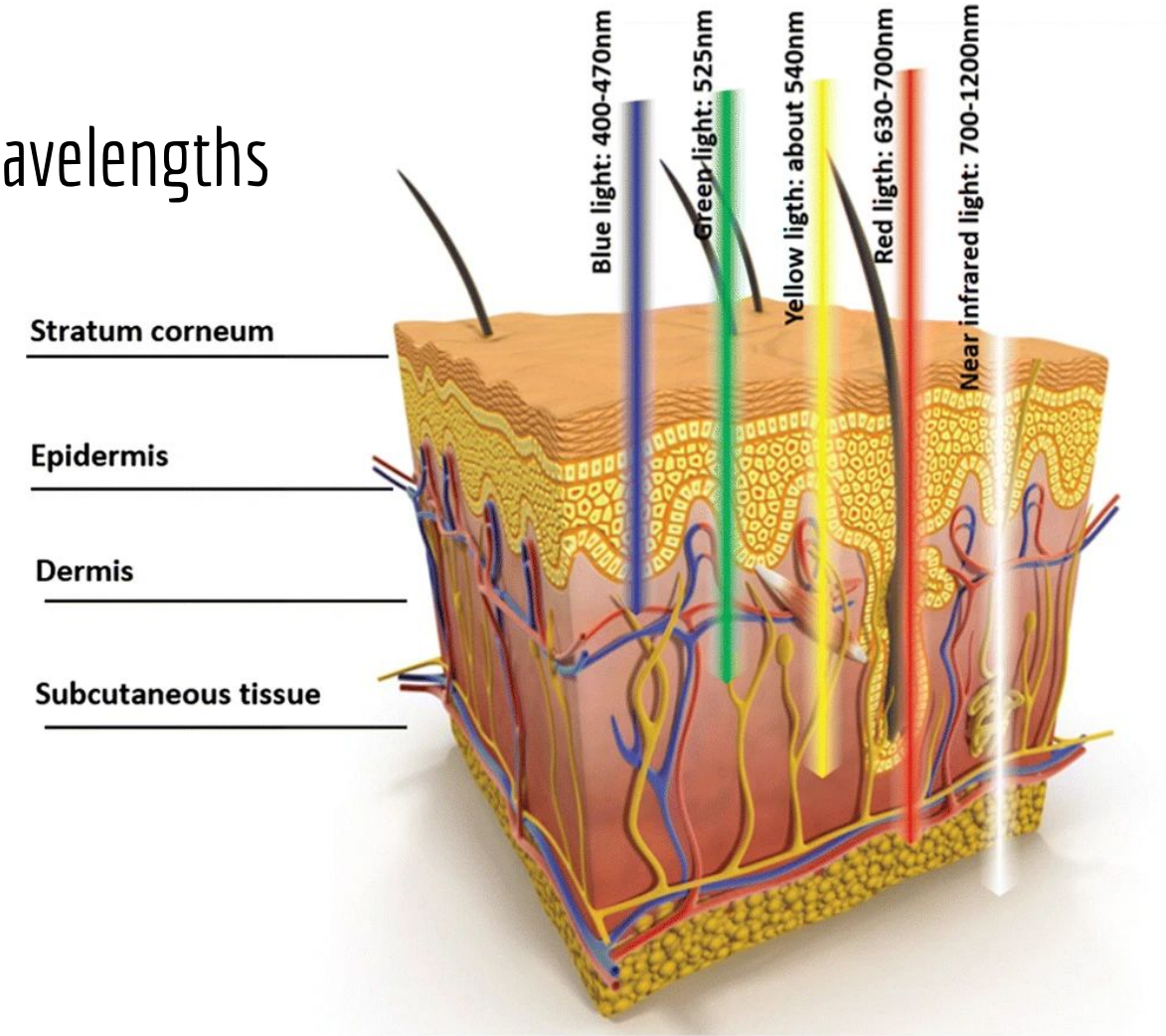
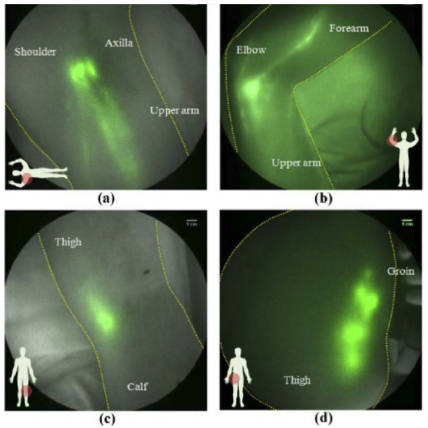
NIR Wavelengths





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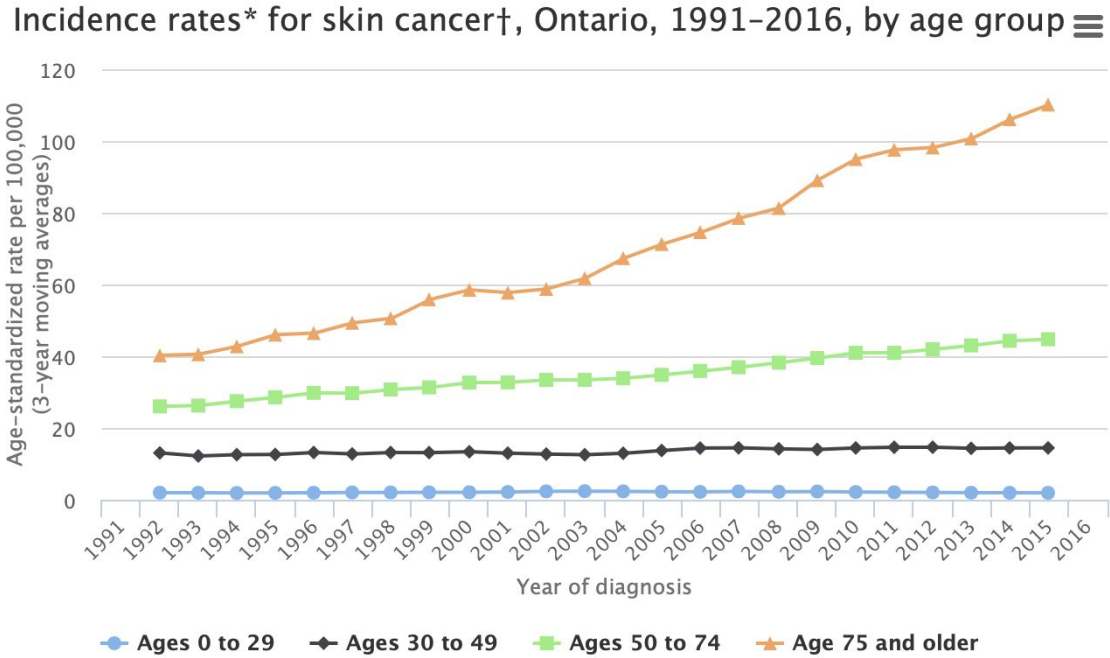
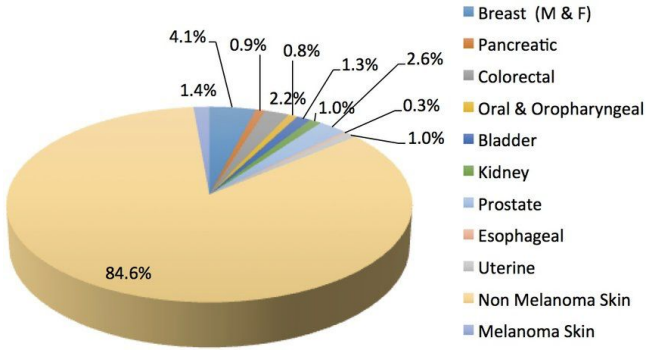
Skin Cancer Diagnostics & Imaging

Over 5,513[19] and 634[20] registered dermatologists, as well as 12,940[21] and 625[22] surgical oncologists practice within the United States and Canada (across 1,200 hospitals).





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Market Need and Size

MolecuLight i:X Market

Leading GPO Accepts MolecuLight i:X Wound Care Device for National Membership

Toronto, CANADA – (June 15, 2020) MolecuLight Inc., the leader in point-of-care fluorescence imaging for real-time detection of bacteria in wounds, announces the availability of its MolecuLight ***i:X***® platform to 9,000 healthcare facilities in the US through its new commercial arrangement with MAGNET GROUP GPO.

MAGNET GROUP is one of the oldest and most experienced Group Purchasing Organizations (GPO) in the US, operating in twenty states and the District of Columbia. MAGNET GROUP solicits and contracts with essential capital medical equipment on behalf of its 9,000 providers, including hospitals, alternate care facilities, physician practices and clinics. MolecuLight is now a registered partner and its ***i:X*** device for detection of bacteria is available to MAGNET GROUP's healthcare members across the US.

MolecuLight Platform is Becoming the Standard-of-Care for Real-Time Imaging of Elevated Bacterial Burden in Wounds Across All Wound Care Settings

TORONTO, CANADA – (October 14, 2021) MolecuLight Inc., the leader in point-of-care fluorescence imaging for real-time detection of wounds containing elevated bacterial loads, announced the launch of the MolecuLight**DX**™, a new point-of-care device model targeted at the unique needs of new expanding wound care market segments in the USA. The **DX** is an expansion of MolecuLight's product line and compliments the MolecuLight ***i:X***®, the "workhorse" wound imaging device that has quickly become a standard in wound care practices worldwide, with over 2,000 units sold.

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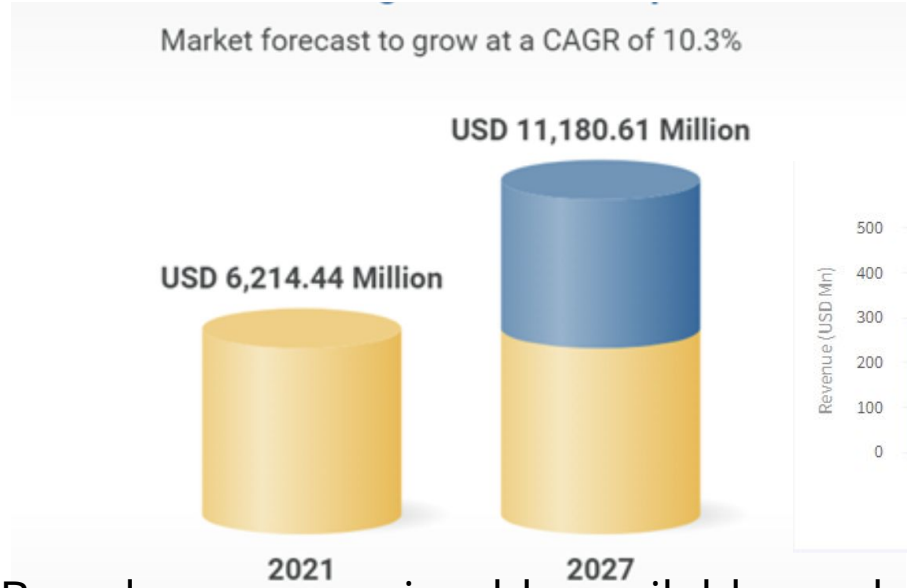
Skin Cancer and Near-Infrared (NIR) Fluorescence Imaging Market



Based on our serviceable available market and high market need, our conservative expectation is a **$5.1 M CDN return on investment**, with net profits annual growth based on an **estimated 4-10% market growth rate.**

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Validation: Biocompatibility, Photobiological Safety

- Literature review supports the safety of ICG and NIR light (Pei et. al., 2020; Sorbellini, et. al, 2018)

- Biocompatibility Testing of Carcinoscope System and ICG
  - Third-Party Testing: NAMSA laboratories (ISO 10993-1:2018 certified)
  - Device categorization: surface device (intact skin) with limited contact duration (<24 hr)
  - ICG: test results will corroborate existing safety data

- Photobiological Safety Testing of NIR light
  - Third-Party Testing: DEKRA (IEC 62471 certified)
  - Assess hazard of NIR on eyes and on skin

Pei, Liu, Y., Liu, Q., Min, X., Yang, Y., Wang, S., Liu, J., Wang, J., & Huang, Y. (2020). The safety and feasibility of intraoperative near-infrared fluorescence imaging with indocyanine green in thoracoscopic sympathectomy for primary palmar hyperhidrosis. *Thoracic Cancer*, *11*(4), 943–949. https://doi.org/10.1111/1759-7714.13345

Sorbellini, Rucco, M., & Rinaldi, F. (2018). Photodynamic and photobiological effects of light-emitting diode (LED) therapy in dermatological disease: an update. Lasers in Medical Science, 33(7), 1431–1439. https://doi.org/10.1007/s10103-018-2584-8

Validation Plan: Clinical Trials

Pilot Trial

Prospective, Single-Blind Phase I/II	
Objective	Feasibility (integrating device into clinical workflow) and Safety
Sample Size (N)	25
Duration	3 months
Primary Outcomes	Skin examination completion rate; Device setup time and variation

Pivotal Trial

Two Arm, Randomized, Cross-Over Phase III	
Objective	Safety and Efficacy compared with RCM and dermatoscopes
Sample Size (N)	400
Duration	19 months
Primary Outcomes	Skin lesion visualization rate; Biopsy accuracy, Tumour recurrence rate

RCM: reflectance confocal microscopy

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Risk & Hazard Analysis

- Standard: ISO 14971:2019
- Hazard categories:
  1) Energy
     i) Mechanical
     ii) Electrical
     iii) Thermal
     iv) Radiation
  2) Biological & Chemical
  3) Performance
  4) Manufacturing

HRI	Levels of Risk	Policies
15 to 25	Unacceptable Risk	Corrective action for hazard severity or probability reduction must be implemented (risk/benefit evaluated as needed).
10 to 14	High Risk	Acceptable as implemented. Risk reduction activities should be implemented.
5 to 9	Medium Risk	Acceptable as implemented. Review as design matures.
1 to 4	Acceptable Low Risk	Acceptable as implemented. Review as design matures.

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Hazard

Device falls onto patient's lesion site.

Causes

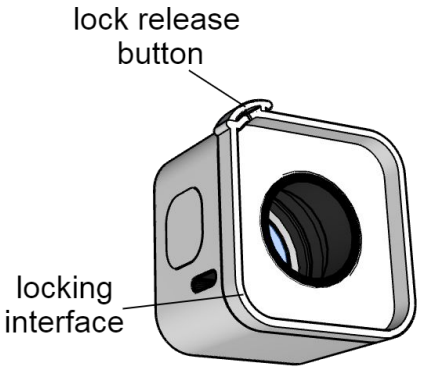
- Improper attachment
- Being top-heavy

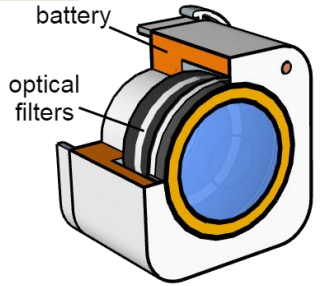
Harms

- Contamination
- Kinetic energy injury

Mitigations

- Auto-lock mechanism
- Audible click
- Compact shape
- Sterilization
- Reduce sharp corners





Hazard

Short circuit & electrical leakage

Causes

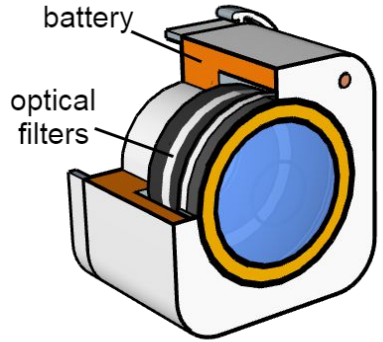
- Disassembled/ damaged battery
- Overheated battery
- Overheated charger
- Excessive humidity

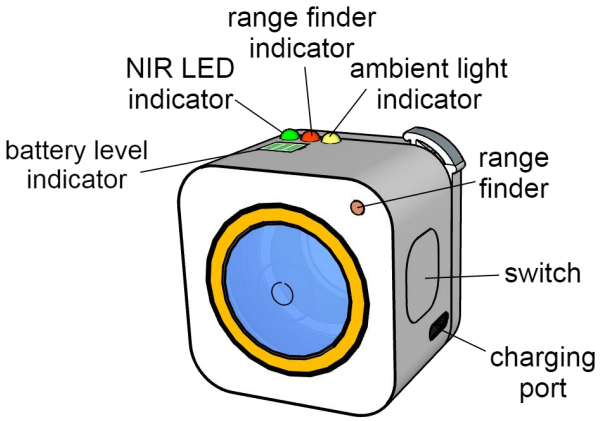
Harm

Electrocution & fire.

Mitigations

- Need special tool to disassemble
- Auto shutdown after 90 seconds
- Charging dock
- Waterproof case





Hazard

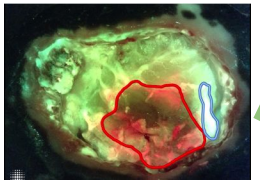
Performance / use errors

Causes

- Broken lens / optical filters
- Light condition not dark enough
- Image taken at wrong distance
- Misinterpret button functionality

Harm

- Misinterpret images



Mitigations

- Gorilla glass attached to lens
- Rubber grip sleeve
- Ambient light sensor
- Range finder indicator
- NIR light indicator
- Clear & permanently printed labels
- Non-diagnostic device
- Pixel intensity tracing algorithm

Residual Risks

HRI	Levels of Risk	Policy
5 to 9	Medium Risk	Acceptable as implemented. Review as design matures.

- All residual risks have a medium or lower risk level (HRI ≤ 9)

Main Residual Risks	S	P	HRI
NIR light prolonged exposure to skin or eyes.	1	3	3
ICG allergy or skin irritation.	4	1	4
Device falls out of user's hand during use.	3	3	9
Internal short circuit.	5	1	5
Overheated battery.	5	1	5
Biological or chemical agents / allergens on surface of device.	5	1	5
Reports have errors.	4	2	8

Design & Development: Project Timeline

- Estimated based on the deliverables at each stage and working efficiency of individuals

H1: January to June
H2: July to December

Market Launch Plan

February 2028

FDA & Health Canada approval
De Novo Pathway

Hospitals & Practitioners

For use of product with money back guarantee

Hospitals & Physicians

Free training sessions

Symposiums, Dermatologist spas. Primary care clinics & Research conferences

Advertise & product placement

Conclusion

Market Need

- Early detection of non-melanoma and melanoma skin cancer
- Imaging devices: few, lack specificity, sensitivity or ability to achieve sufficient tissue depth to consistently detect skin lesions

Unique Product

- Real-time diagnostic and intraoperative procedures in the early detection and monitoring skin cancers
- Flexibly interact with and retains the intended use of the MolecuLight i:X device

Risks

- Device falling, electrical-related, user-related risks
- All residual risks HRI<9

Benefits

- Improve early detection of skin lesions
- Reducing healthcare expenditure
- Transform current screening strategies

THANK YOU

Any questions?