Ministry of Foreign Affairs

Matching Dutch Solutions to Minnesota's Medical Alley

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Matching Dutch Solutions to Minnesota's Medical Alley

Opportunity Assessment, Strategic Recommendations, Next Steps

April 29, 2021

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Executive summary

Executive summary

- Medical Alley's commercial strength in medical devices has roots in the University of Minnesota's groundbreaking advancements in cardiac surgery and rhythm management in the 1950s. U of MN researchers collaborated with area entrepreneurs on new devices such as the first battery-operated pacemaker (the origin of Medtronic) and the first bi-leaflet valve (the origin of St. Jude Medical).
- Medical Alley's distinctive healthcare environment was shaped by the Mayo Clinic, which developed a multidisciplinary, patient-centered approach to care that remains the country's model for healthcare reform. Mayo has been consistently ranked as the nation's top hospital and the Mayo network is Minnesota's largest employer. Minnesota is ranked ahead of Boston in effectiveness of care and in hospitals and ambulatory surgical centers.
- Today, the Medical Alley region is second only to Boston and Chicago in overall annual sales of medical devices and contains the greatest number of publicly held medical device companies in the United States. Four of the nation's top 10 medical device companies—Medtronic, 3M Healthcare, Boston Scientific, and St. Jude Medical--are headquartered or have a strong presence in Medical Alley.
- Medical Alley's strength is medical devices. Driven by decades of innovation from the Mayo Clinic, and the University of Minnesota, and the region's medtech giants, Medical Alley leads all other U.S. medtech clusters in patents specific to "medical device" and is a major recipient of NIH funding for MRI and AI research. The Mayo system is a global innovator in both healthcare and medtech, with nearly $1B in annual research funding.
- Whereas medtech incubators San Diego and Silicon Valley exceed Medical Alley in venture capital funding, much of the innovation that takes place in Medical Alley is funded by corporate investment in research and development. In 2020, Medical Alley's top three medtech companies invested $3.1B in R&D, compared with a national total of $4.2B in venture capital funding for medical devices.
- Medical Alley is supported by a vast ecosystem of contract manufacturers, device testing outfits, designers, and regulatory and product development consultants. More than 32,000 Minnesotans are employed in the medical device industry, second only to California.

Executive summary, continued

- Medical Alley's collective medical device experience has made it highly efficient in medtech commercialization. Between 1960 and 2014, fully one third of U.S FDA medical device premarket approvals were obtained by Medical Alley companies. A study of time to clearance for 510K and PMA medical devices between 2010 and 2014 found that Medical Alley 510Ks clearances were 26% faster than the national average, while premarket approvals in Medical Alley were 6.5 months faster.

- Led by Medtronic, Medical Alley's medical device giants are investing heavily in acquiring artificial intelligence technology to differentiate and improve the performance of their medical imaging, surgical robotics, neuromodulation, wearable monitoring, disease detection, and other products. Regional giant 3M Healthcare recently spent $1B to acquire AI technology to improve its software platforms for physicians and hospitals. The Mayo Clinic has entered into a 10-year collaboration with Google to enhance clinical practice with AI. Dutch strength in AI applications for medtech and healthcare systems could also be of significant interest to Medical Alley medtech companies and the region's hospital-based healthcare network.

- In interviews conducted for this project, area thought leaders in medical imaging, 3D printing/robotics, and clinical diagnostics highlighted several area needs that could be addressed by Dutch medtech strengths. These include improved AI integration, signal to noise ratios, and sensitivity in imaging; incorporation of tactile sensors into surgical robotics products; and improved systems for 3D printing of microfluidics for handheld diagnostic devices.

- Dutch strengths in AI, neurology, materials science, microchip fabrication, and wireless power and communications are well matched to the needs of Medical Alley medtech giants for improving surgical robotics, disease detection, and brain/pain therapies (Medtronic); wearable AI-assisted monitoring (Boston Scientific); and AI-assisted medical imaging (St. Jude). Dutch strength in applying AI and machine learning to identify ideal treatments for individual patients and to improve healthcare ecosystems match well with similar initiatives at 3M, as well as with the Mayo Clinic's continued focus on AI-assisted healthcare improvement.

- The key to success for Dutch companies interested in engaging with Medical Alley is making direct contact with area thought leaders. The Medical Alley organization is ideally suited to facilitate such contacts and can be used for matching "mentors" to Dutch startups and SMEs. Dutch medtechs should also establish contacts with researchers at the U of MN and Mayo and seek opportunities to prove out their products in Minnesota's well-regarded hospitals, which have a tradition of collaboration with industry. Organizing customized tours to Medical Alley could be of significant benefit.

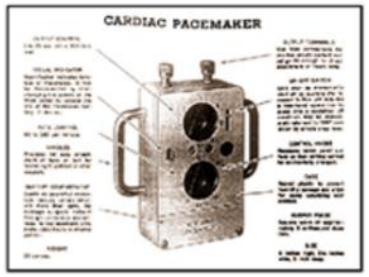
Medical Alley as a medtech sector

Medical Alley's roots: advancements driven by academic/industry collaboration

University of Minnesota
Driven to Discover®

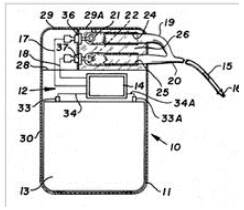
Pioneering work in cardiovascular medicine at the University of Minnesota underlies the development of today's Medical Alley giants.

Medtronic



Dr. Lillehei asks device repairman Earl Bakken for a battery-operated cardiac pacemaker. He develops it in his garage – and later founds **Medtronic.**
1958

CPI



Cardiac Pacemakers, a Medtronic spin-off, founded to market the world's first lithium-powered pacemaker. Initial market cap: $50,000
1972

ST. JUDE MEDICAL

St. Jude Medical founded to produce bi-leaflet values
1976

Today, Medical Alley is best known for cardiac rhythm management and interventional cardiac devices and imaging, with a growing focus on AI, remote monitoring, and robotics

Boston Scientific

Cardiac Pacemakers later becomes **Guidant**. Guidant purchased by **Boston Scientific** for $27B
2006

Abbott

Abbott buys **St. Jude** and its portfolio in atrial fibrillation, heart failure, structural heart, and chronic pain for $25B
2017

1950

First open-heart surgery using hypothermia, Dr. JF Lewis, U of MN
1952

First cardiopulmonary bypass, Dr. CW Lillehei, U of MN
1953

Artificial bi-leaflet valve invented at U of MN
1972

Dr. Gibbon pioneers the heart-lung machine using his "bubble oxygenator" (cost: $15)

Visible Heart Laboratory founded, U of MN
1997

U of MN Earl E. Bakken Medical Device Laboratory founded
2008

2020

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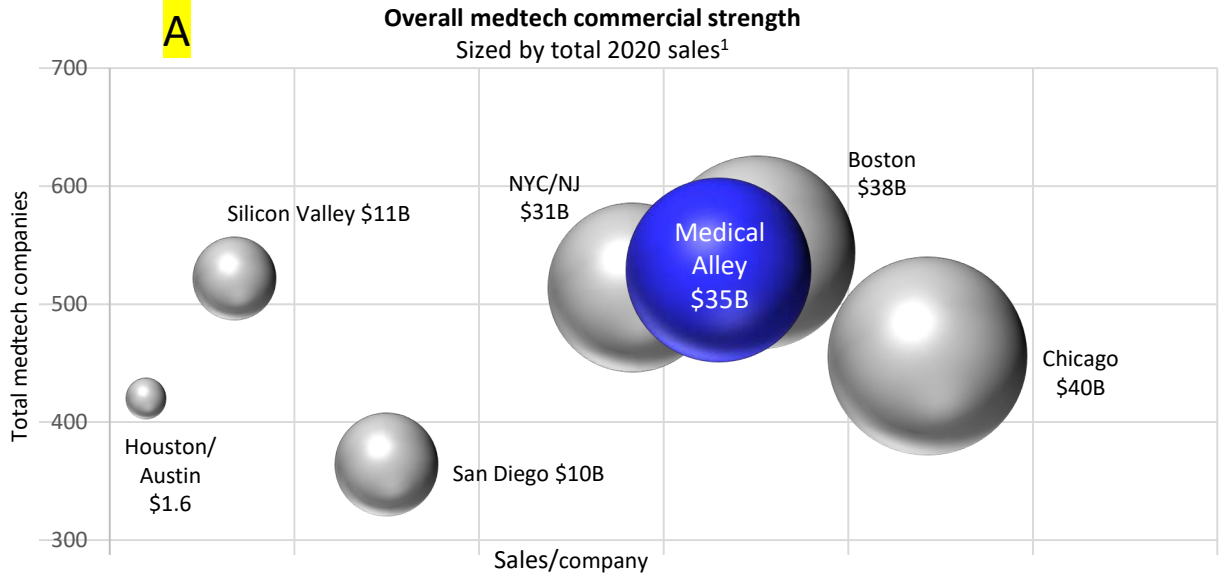
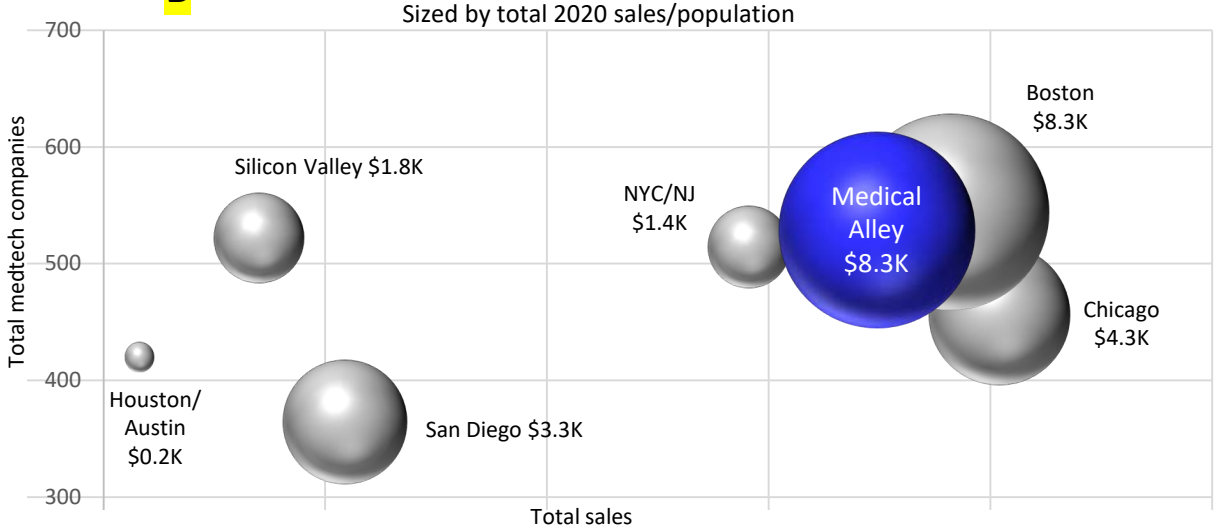
Today, Minnesota's Medical Alley is a medtech heavyweight

A

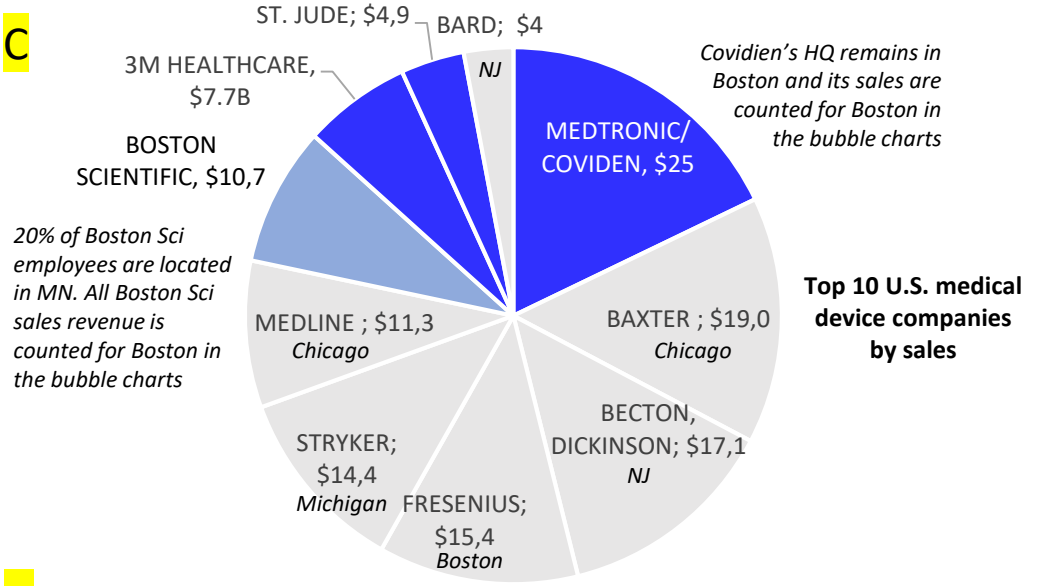


B

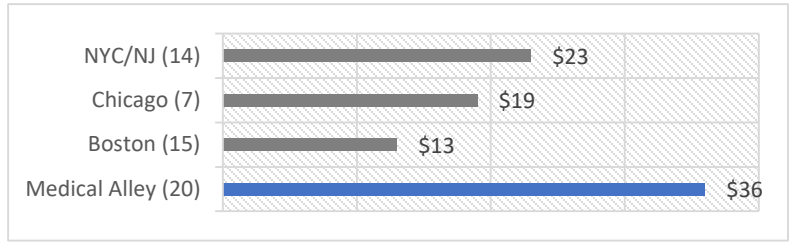


In terms of commercial strength assessed by sales for medtech companies (NAICS 339112, 339113), the Minneapolis/St. Paul and Rochester, MN, areas exceed all other U.S. regions but greater Chicago and Boston (A). Medical Alley equals Boston in concentration of medical device commercial strength (B). Medical Alley contains four of the top 10 U.S. medical device companies (C) and the greatest number of publicly held medical device companies (D).

C



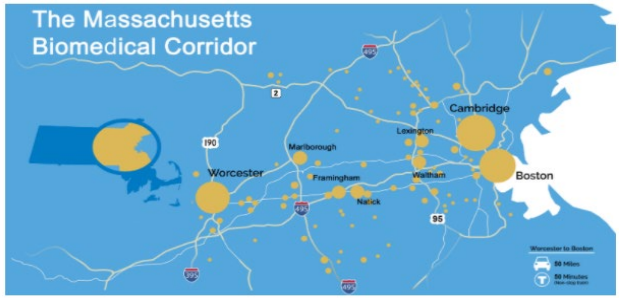
D



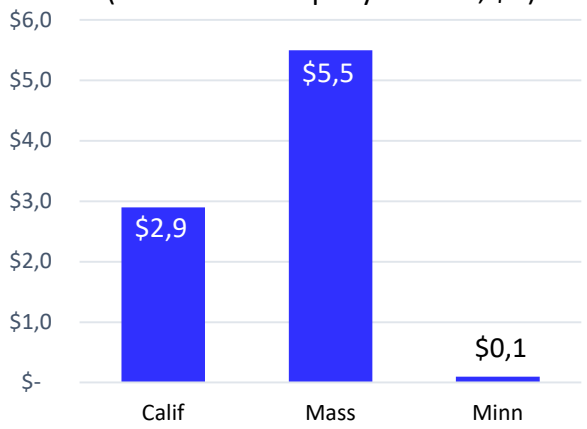
1 Mergent Intellect database, NAICS codes 339112 and 339113

Minnesota is about devices, not biotechnology (for now)

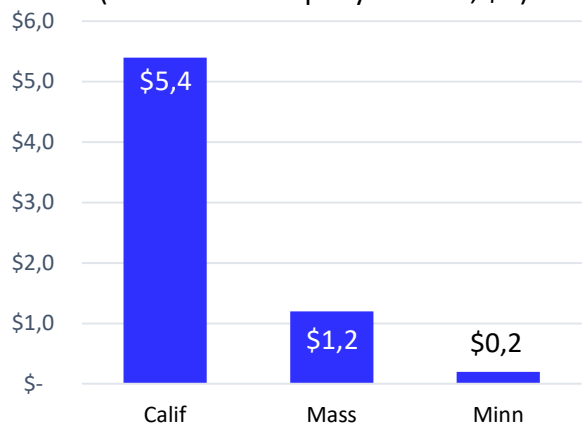
The coasts drive innovation in biotechnology. California and Massachusetts lead in biotechnology know-how related to clinical diagnostics (genomes, assays; below) with Boston leading in 2020 income generated by biotechnology R&D companies (right).



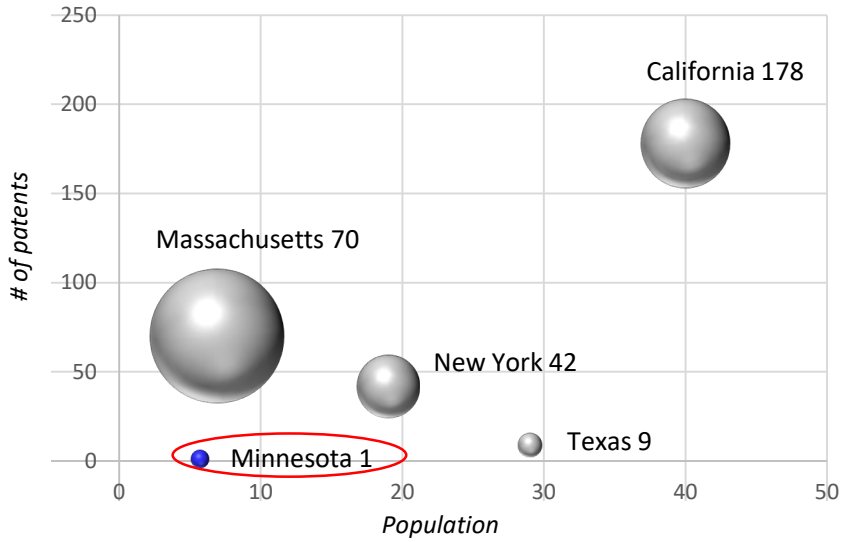
Biotechnology R&D
(Combined company income, $B)[2]



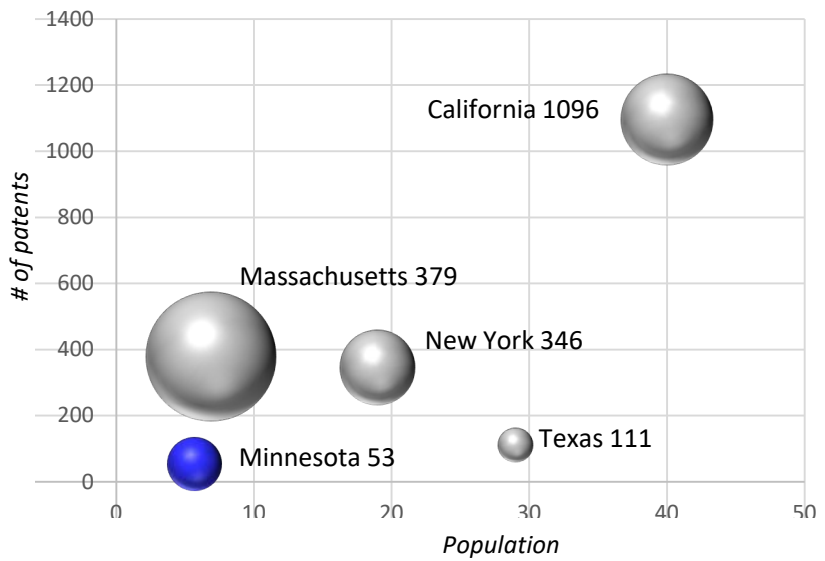
Medical labs & diagnostic imaging centers
(Combined company income, $B)[3]



"Genome" patents, 1976—2020[1] (sized by pats/M pop.)



"Assay" patents, 1976—2020[1] (sized by pats/M pop.)



Bright spot on the Minnesota landscape. The Minnesota Partnership for Biotechnology and Medical Genomics, a collaboration among the Mayo Clinic, the University of Minnesota and state government, has attracted more than $60 million in grants from the NIH.

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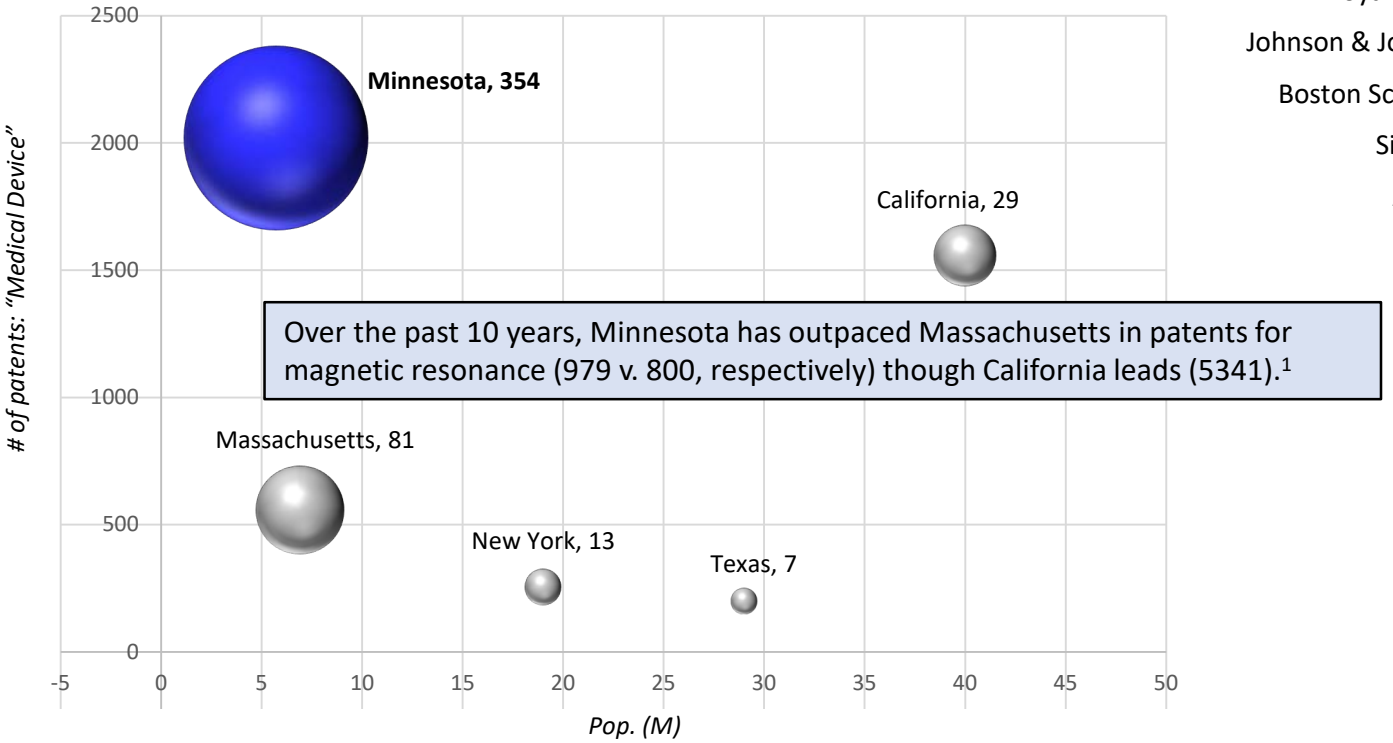
1 Patentsview.org 2021
2 Mergent Intellect database, 2021 NAICS code 541714
3 Mergent Intellect database 2021, NAICS codes 621511, 621512

Medical Alley: medical device funding and brainpower

Medical Alley leads the nation in medical device know-how. Driven by decades of innovation from Medtronic, Mayo, and the U of MN, Minnesota leads the U.S. in medical device patents, in terms of both overall patents and density of patents by population.[1]

Over the past 10 years, Minnesota has outpaced Massachusetts for patents in **magnetic resonance imaging** (979 v. 800, respectively) though California leads (5341).[1]

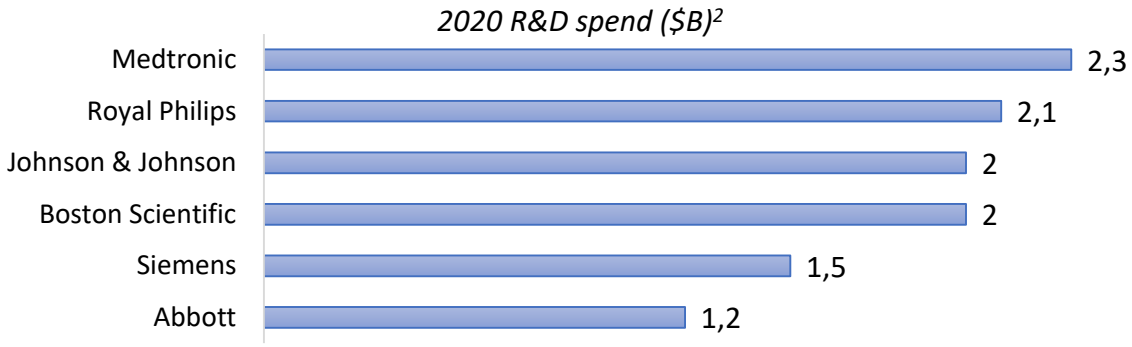
Patents: "medical device," 1976—2020[1] (sized by pats/M pop.)*



Over the past 10 years, Minnesota has outpaced Massachusetts in patents for magnetic resonance (979 v. 800, respectively) though California leads (5341).[1]

* These comparisons do not reflect all medical device patents, only those issued that include the specific words in " ". They are meant for broad comparisons only.

Medical device innovation is well-funded in Medical Alley. Medtronic leads the global medical device industry in research and development spending (below). Two of the remaining top spenders in R&D (Boston Scientific and Abbott) have a strong presence in Medical Alley.



The Earl E. Bakken Medical Devices Center *at the U of MN is an interdisciplinary program that combines basic research, applied and translational research, education and training.*

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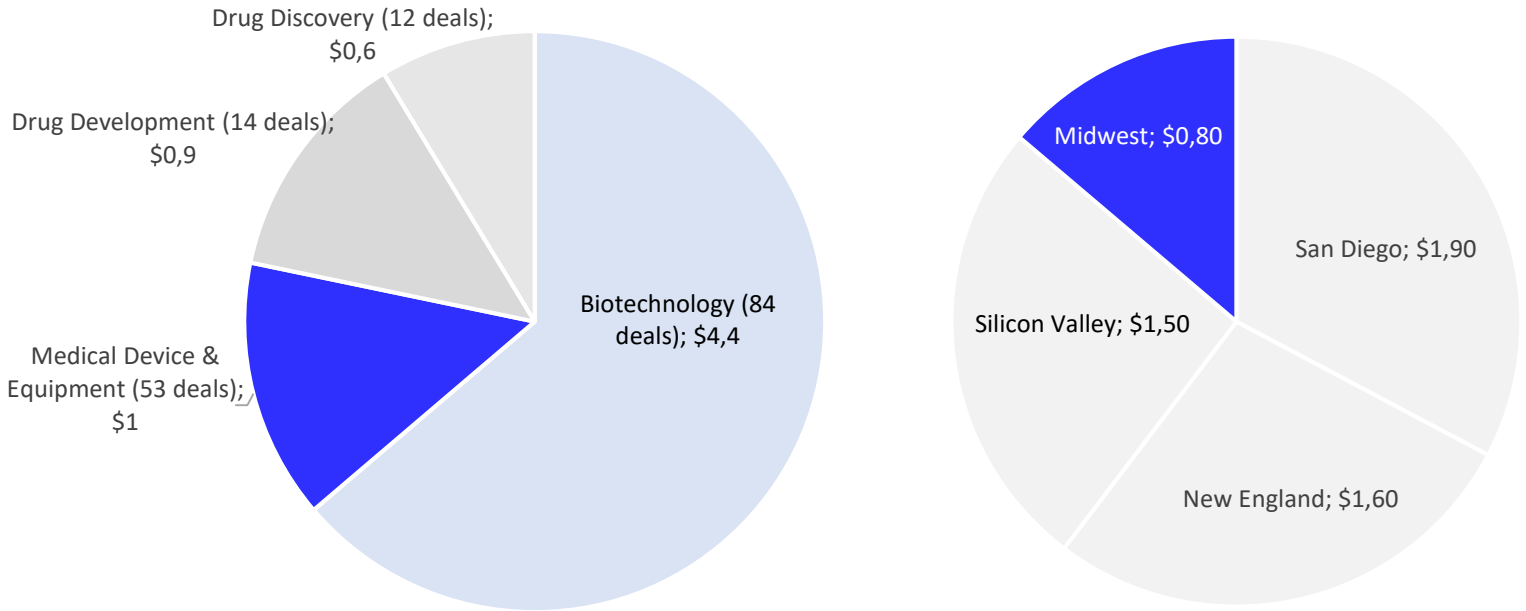
1. Patentsview.org, 2021
2. Medical Design & Outsourcing, 2021.

Medical Alley is about corporate R&D investment, not VC funding

In terms of VC dollars invested in healthcare companies, biotechnology continued to lead in Q4'20.*
The Medical Devices & Equipment industry outperformed the Drug Development industry in dollars invested and number of deals, with $1B dollars invested and 53 deals closed (below).*

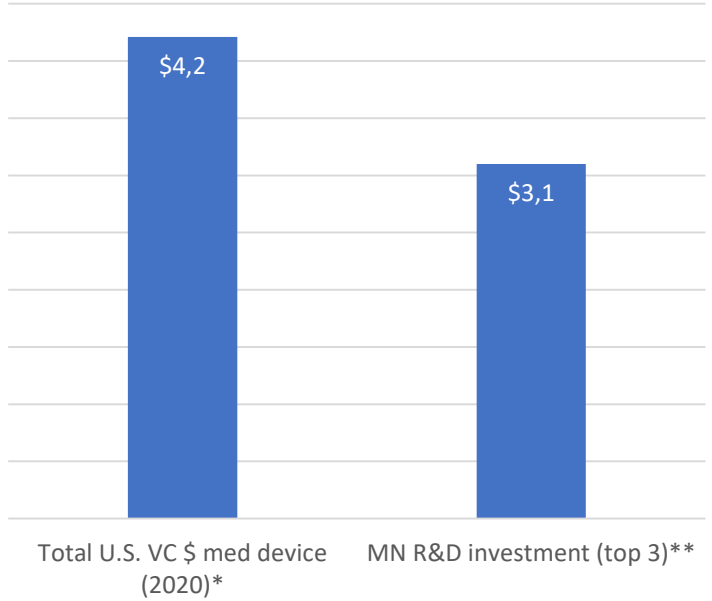
In 2020, estimated Medical Alley R&D investment among its top 3 medtech companies equaled three quarters of the total U.S. venture capital investment in medical devices (below, right).

Venture capital investment in healthcare
($B, Q4 2020)*



Medtronic 3M Boston Scientific

U.S. VC medical device funding vs. est. MN medical device corporate investment in R&D ($B)
Medtronic, 3M HC, Boston Scientific



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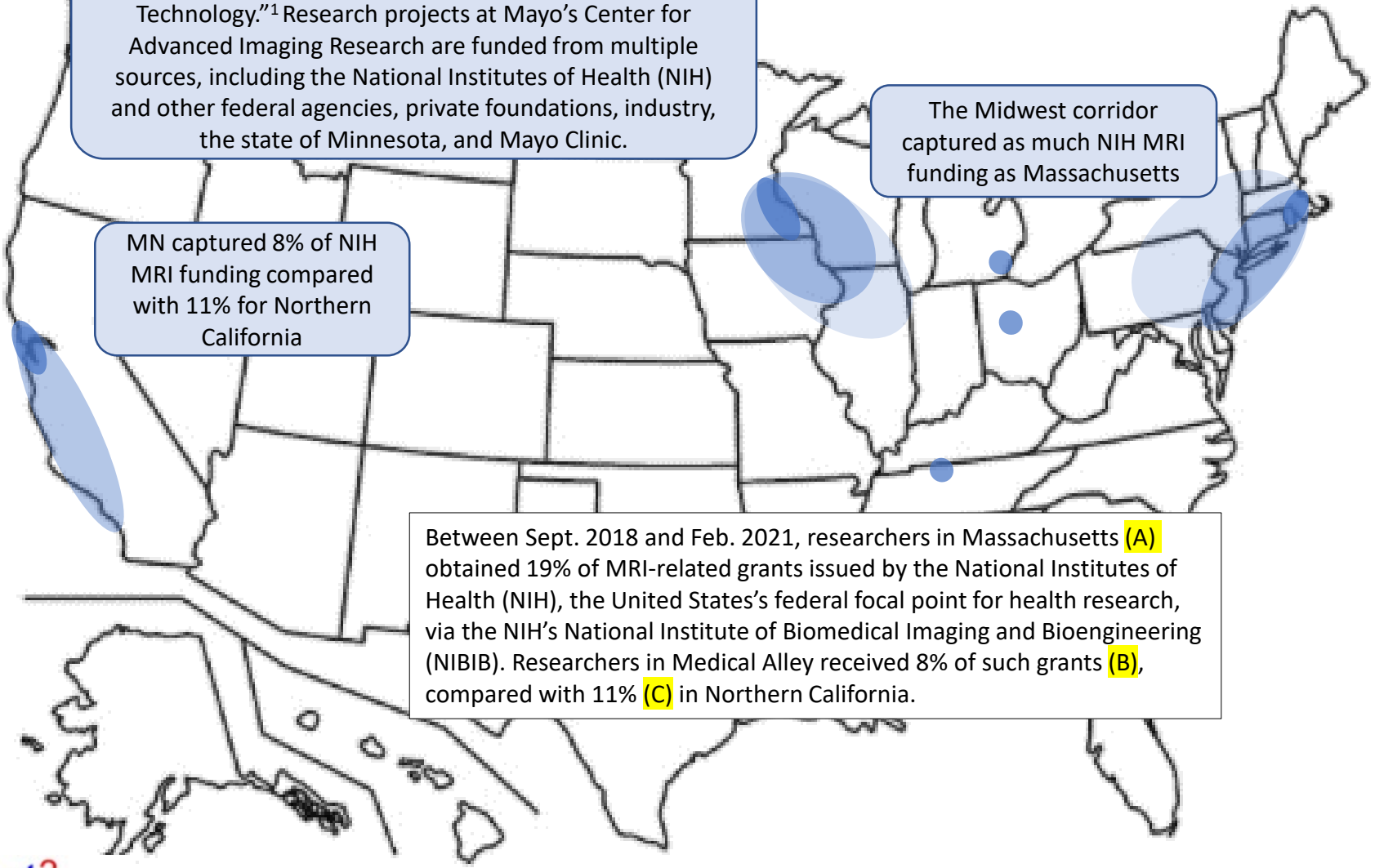
* Healthcare Moneytree Report, Q4 2020
**3M HC R&D calculated from total 3M R&D spend/HC share of total revenue; Boston Scientific calculated from total R&D spend * % of MN employees (20%)

Medical imaging brainpower: recent federal research grants in MRI

"Nearly every MRI machine contains Mayo Clinic Technology."[1] Research projects at Mayo's Center for Advanced Imaging Research are funded from multiple sources, including the National Institutes of Health (NIH) and other federal agencies, private foundations, industry, the state of Minnesota, and Mayo Clinic.

The Midwest corridor captured as much NIH MRI funding as Massachusetts

MN captured 8% of NIH MRI funding compared with 11% for Northern California



Between Sept. 2018 and Feb. 2021, researchers in Massachusetts (A) obtained 19% of MRI-related grants issued by the National Institutes of Health (NIH), the United States's federal focal point for health research, via the NIH's National Institute of Biomedical Imaging and Bioengineering (NIBIB). Researchers in Medical Alley received 8% of such grants (B), compared with 11% (C) in Northern California.

This program supports the technological development of in vivo MR imaging and MR spectroscopy, for both animal and human research and potential clinical applications.[2]

	EAST					
A	MASS	26	19%	19%		
	NY	16	11%		41%	46%
	Balt	11	8%			
	Conn	4	3%			
	Del	1	1%			
	Penn	7	5%			
	MIDWEST					
B	U Mn	7	5%	8%	11%	18%
	Mayo	4	3%			
	U Iow	2	1%			
	U Wis	3	2%			
	U ILL	9	6%			
	WEST					
C	N Cal	16	11%	11%	12%	
	S Cal	2	1%			

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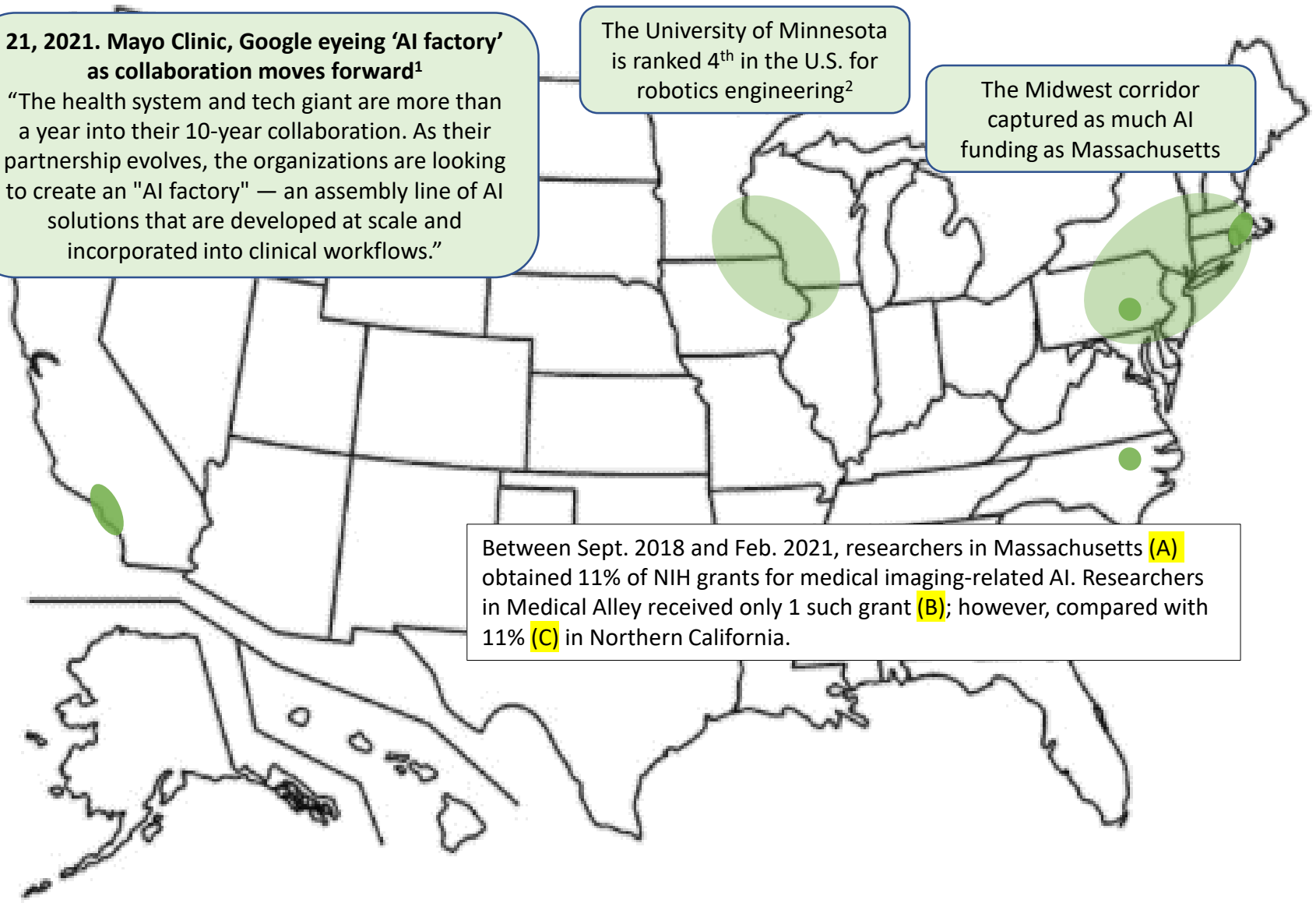
1. Mayo Clinic. About Mayo Ventures. http://ventures.mayoclinic.org/about.php
2. NIH NIBIB research grants Sept. 2018–Feb. 21, 2021

AI brainpower: recent federal grants in AI for medical imaging

21, 2021. Mayo Clinic, Google eyeing 'AI factory' as collaboration moves forward[1]
"The health system and tech giant are more than a year into their 10-year collaboration. As their partnership evolves, the organizations are looking to create an "AI factory" — an assembly line of AI solutions that are developed at scale and incorporated into clinical workflows."

The University of Minnesota is ranked 4th in the U.S. for robotics engineering[2]

The Midwest corridor captured as much AI funding as Massachusetts



Between Sept. 2018 and Feb. 2021, researchers in Massachusetts (A) obtained 11% of NIH grants for medical imaging-related AI. Researchers in Medical Alley received only 1 such grant (B); however, compared with 11% (C) in Northern California.

This program supports the design and development of artificial intelligence, machine learning, and deep learning to enhance analysis of complex medical images and data.[3]

	EAST				
A	MASS	3	11%		
	NY	1	4%	21%	32%
	Balt	1	4%		
	Conn	1	4%		
	Penn	3	11%		

	MIDWEST				
B	U Mn	0	0%	4%	11%
	Mayo	1	4%		
	U Iow	1	4%		
	U Wis	1	4%		
	TOTAL	3			

	WEST		
C	S Cal	5	18%
	TOTAL	5	

1 MedCity News. Feb. 21, 2021. https://medcitynews.com/2021/02/mayo-clinic-google-eyeing-ai-factory-as-collaboration-moves-forward/?rf=1
2. Wonderful Engineering, 2020
3. NIBIB research grants (artificial intelligence) Sept. 2018–Feb. 21, 2021

The Medical Alley medtech landscape

Medtronic
Cardiovascular, surgical, diabetes, neurological, spinal devices

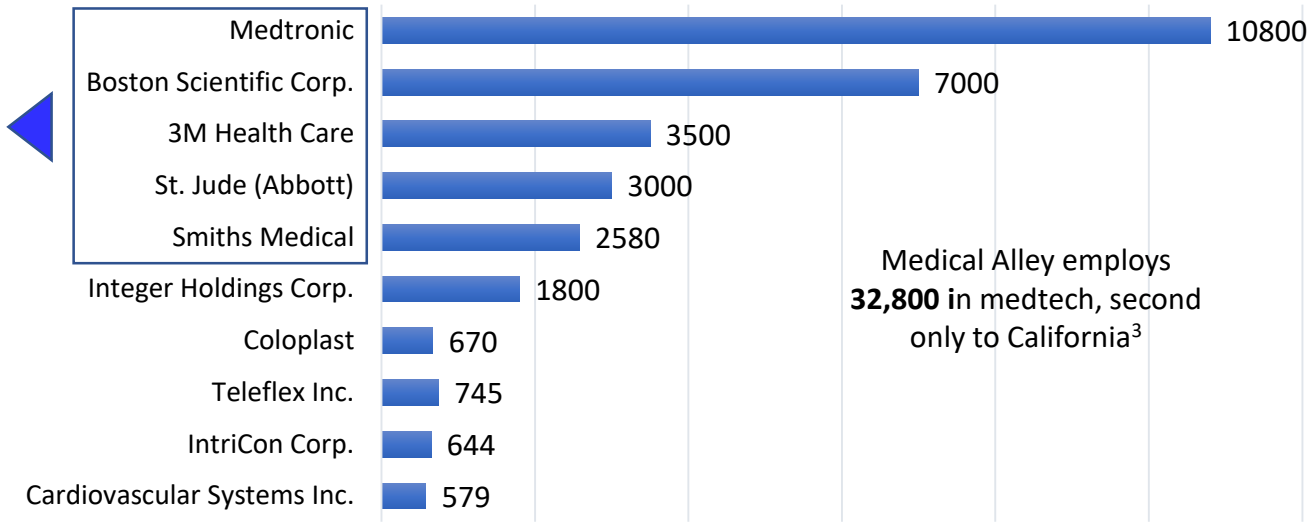
Boston Scientific
Interventional radiology, cardiology, vascular, neuromodulation, electrophysiology, and more

3M Healthcare
Surgical safety, infection prevention, patient temp. reg., sterilization and reprocessing, drug-delivery devices and supplies

St. Jude (Abbot)
Cardiovascular devices and imaging systems, neurostimulation devices

Smiths
Infusion pumps, health-monitoring technology, catheters and ventilators, devices and consumables for patient care

Number of Minnesota employees[1]



Medical Alley employs **32,800** in medtech, second only to California[3]

Integer
Electrochemical engineering; develops and manufactures surgical tools and parts for medical devices like pacemakers

Coloplast
Ostomy care, continence care, wound and skin care, urology care

Teleflex
Interventional medical devices for cardiologists, radiologists, electrophysiologists and vein practices

IntriCon
Body-worn bio-telemetry devices, hearing instruments and professional audio communications devices

Cardiovascular Systems
Minimally invasive treatment solutions for vascular disease

Medical Alley is also the U.S. HQ of **Stratasys**, a global top 10 in medical 3D Printing[4]

Medical imaging *Clinical diagnostics* *Robotics* *AI* ***Key strategic focus[2]***

1. Variety of 2020/2021 sources. 3M is estimated based on # of MN employees/% of HC business
2. Investor relations documents
3. Minnesota DEED, Compare Minnesota, 2021
4. Dr. Hempel Digital Healthcare Network. Top 10 companies in medical 3D printing. 2021.

The Medical Alley medtech landscape: key suppliers

Ametek Engineered Medical Components
Surgical and Medical Instruments[1]

Composed of 3 businesses: Avicenna, Technical Services for Electronics, and Laserage (OEM med devices)
Single-site location in MN (parent company Ametek, PA)

2020 sales[2]	$267M
Employees[2]	500-1000

Capabilities of special interest:
Optical technologies
- Customized ultrasound solutions for cardiology and radiology
- Intravascular ultrasound and intracardiac echocardiography (ICE) catheters

Electrophysiology
- Mapping and sensing electrodes

Neuromodulation
- Implanted lead conductors

Phillips-Medisize
Plastics product manufacturing[1]

"Global leader in connected health"
Multi-site locations with HQ in Hudson, WI (bordering MN)

2020 sales[2]	$750M
Employees[2]	5400

Capabilities of special interest:
AI and monitoring
- Customized systems for collection and analysis of patient data related to diagnosis and medication adherence

IoT
- Data connectivity for a variety of medical devices (e.g., drug injection devices)

Clinical diagnostics
- Rapid point of care diagnostic tests
- Diagnostic kits for home use

Nortech
Electronic Component Manufacturing[1]

Wire and cable assemblies, printed circuit boards, electronic components
Single-site location in MN

2020 sales[2]	$104M
Employees[2]	728

Capabilities of special interest:
Optical technologies
- "The premier producer of camera cable and assemblies in the United States"
- "Intercon 1 by Nortech has been the leader in machine vision technology for decades."
- Supplier to GE Healthcare for medical imaging components

IoT
- Strong strategic focus on "connectivity"

Design/development
- Acquired Devicix for upstream electromechanical med device design

Minnetronix
Electrical Equipment and Component Manufacturing[1]

Complete Medical Device Commercialization Services Including Design & Manufacturing
Single-site location in MN

2020 sales[2]	$44M
Employees[2]	135

Capabilities of special interest:
Visualization
- Optical Coherence Tomography (OCT)
- AI/machine learning

Diagnosis
- Optical measurement
- Diagnostic lasers

Diagnostics and Monitoring
- Wearable sensor-based devices
- Optical, EM and motion sensors
- Data, app, cloud and AI capability
- Data, compliant security and encryption, cloud and AI

Complex fluids systems integration

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Medical imaging *Clinical diagnostics* *Robotics* *AI*

1. Primary NAICS code
2. Mergent Intellect database, 2021

The Medical Alley medtech landscape: other major area suppliers

Cirtec Medical
Surgical and Medical Instrument Manufacturing[1]

Design/development of precision components and finished device (active implants, minimally invasive therapeutic devices.
Multi-site locations with HQ in MN

2020 sales[2]	$80M
Employees[2]	900

Capabilities of special interest:
- Leadless implantable pacemakers
- Implantable drug delivery
- MR safety testing

Integer
Capacitor, Resistor, Coil, Transformer, and Other Inductor Manufacturing[1]

One of the world's largest medical device outsource manufacturing companies
Multi-site locations with HQ in Texas

2020 sales[2]	$1B
Employees[2]	8250

Capabilities of special interest:
Implantable medical devices
- Pacemakers
- Defibrillators
- Pulse generators (neurostim)
- Batteries

IntriCon
Electronic Component Manufacturing[1]

Precision microminiature components and molded plastic parts, such as volume controls and switches, primarily used in hearing aids.
Multi-site locations with HQ in MN

2020 sales[2]	$102M
Employees[2]	670

Capabilities of special interest:
- Cardiac monitoring patches
- Continuous glucose monitoring (CGM) systems
- Gastrointestinal capsules that a patient can swallow to capture images or collect sample bacteria in the GI tract
- Proprietary wireless technology

Donatelle
Medical device contract manufacturing

Design, development and manufacture of intricate medical devices and components – including high-risk, long-term implants and disposables – where precision, tolerances, validation and timelines are vital.

2020 sales[2]	N/A
Employees[2]	130

Capabilities of special interest:
- Microfluidics for clinical diagnostics
- Point of care diagnostics
- Laparoscopic and minimally invasive devices; ophthalmic surgical devices
- Neurostimulation products: cochlear implants, leads, neurostimulators
- Implantable cardiac monitoring
- Cardiac rhythm management devices

Medical imaging *Clinical diagnostics* *Robotics* *AI*

1. Primary NAICS code
2. Mergent Intellect database, 2021

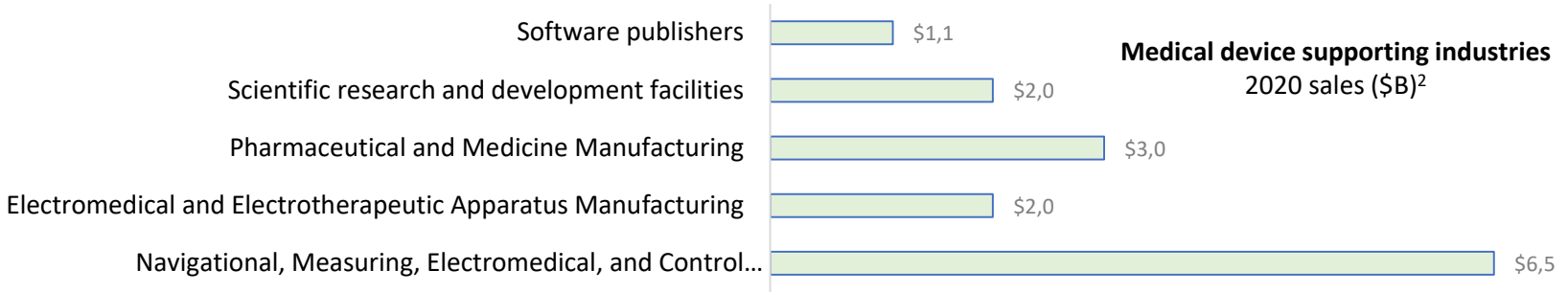
Bottom line: For Dutch medtech, Medical Alley is not flyover country

"Minnesota arguably has the institutions and the talent required to provide the U.S. healthcare industry the innovation it desperately needs. The question is whether potential investors will notice the hub nicknamed 'Medical Alley.'"
Medical Design & Outsourcing, 2020[1]

#2 Medical device state[1]

MD&O ranks **Minnesota** (pop. 5.7M) the #2 medical device state, exceeded only by **California** (pop. 40M)

Medical Alley has a vast ecosystem of contract manufacturers, device testing outfits, designers, and regulatory and product development consultants. More than 32,000 Minnesotans are employed in the medical device industry, twice as many as Massachusetts.[1]



Medical Alley's UnitedHealth is the nation's largest private health insurer (by net premiums)

Medical Alley leads the nation in speed to FDA clearance for medical devices,[3] with resources developed over decades of high-volume experience in clinical trials and FDA clearances

33% of all U.S. premarket approvals between 1960-2014[3]

26% faster first 510K clearances than the US average – a 30-day advantage.[3]

6.5-month faster first PMAs than the US average.[3]

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1 Medical Design & Outsourcing, 2020.
2. Mergent Intellect Database, 2020
3. Evaluate Medtech, 2015

Medical Alley means efficiency in FDA clearance

Evaluate Medtech

In 2015, Minnesota's Life Science Alley organization (now called Medical Alley) commissioned independent market research company Evaluate Medtech to examinate average time to FDA clearance (510K and PMA) for U.S. states.[1,2]

In 2010, the average cost/month of a PMA pivotal trial was $1.4 M[3]

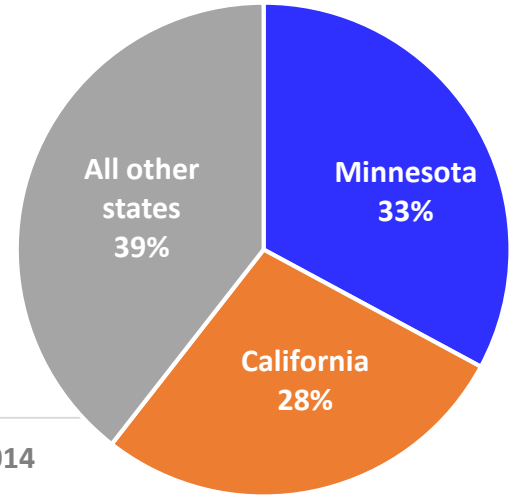
Efficiency born of experience

"California is home to more medical device companies than any other U.S. state...but some of the most life-saving (as well as most highly regulated) devices have been created in Minnesota."[4]

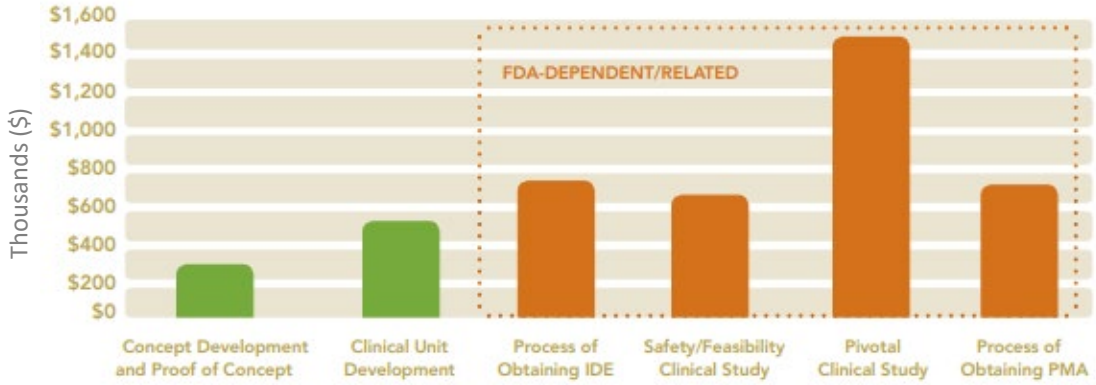
NAMSA

NAMSA, a $200M clinical research organization with a strong presence in MN, is 100% focused on medical devices. In March 2021 they acquired American Preclinical Services to expand their breadth of service.

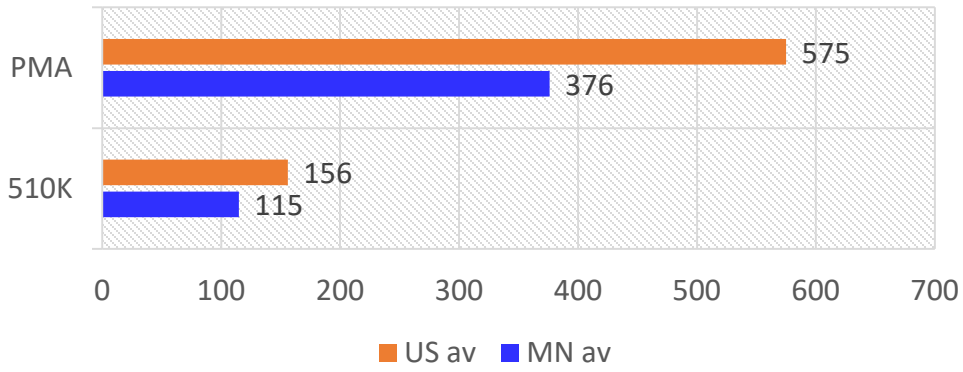
Total PMA clearances 1960 – 2014[2]



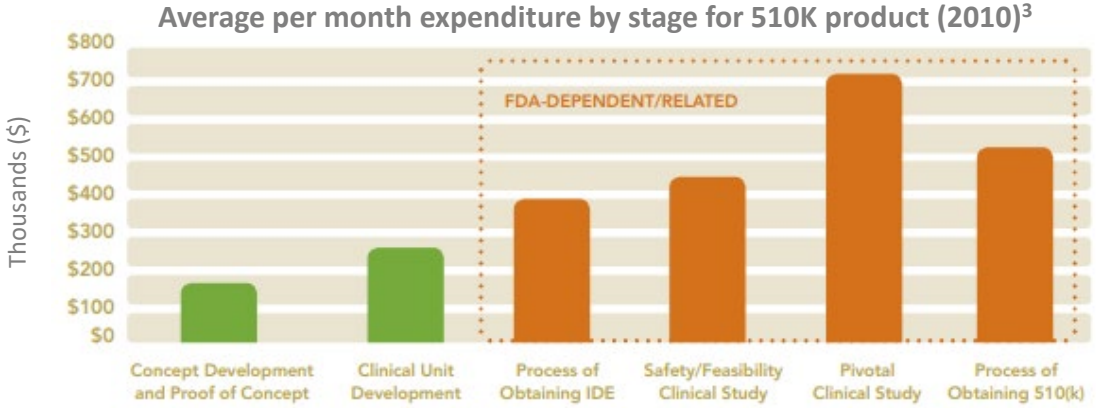
Average per month expenditure by stage for PMA product (2010)[3]



Time to FDA clearance (av. Days) – 2010-2014



Average per month expenditure by stage for 510K product (2010)[3]



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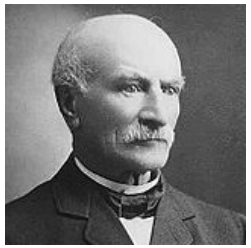
1. Minnesota Fastest in Nation in 510K Approvals. Life Science Alley, 2015.
2. Minnesota Fastest in Nation in PMA Approvals. Life Science Alley, 2015
3. AdvaMed FDA Impact on U.S. Medical Technology Innovation, 2010.
4. Medical Design & Outsourcing, 2020.

Medical Alley as a healthcare sector

Medical Alley's care system has been shaped by Mayo

Medical Alley's innovative and collaborative, hospital-based care system has roots in the Mayo Clinic. Today, the Mayo healthcare network remains the largest in Minnesota.[1,2]



Dr. William James Mayo moves his practice to Rochester to serve the Union Army in the Civil War

When a tornado strikes Rochester, Dr. Mayo is placed in charge of organizing medical care. Needing nurses, he reaches out to nun Mother Alfred Moes, who later proposes they raise funds for a hospital.

Ranked 1st
Diabetes and Endocrinology
Gastroenterology
Geriatrics
Gynecology
Nephrology
Neurology and Neurosurgery
Pulmonology
Urology

Ranked 2nd
Cardiology and Heart Surgery
Ear, Nose and Throat
Orthopedics

Ranked 3rd - 6th
Cancer (3rd)
Rheumatology (4th)
Psychiatry (5th)
Rehabilitation (6th)

"Throughout its 140-year history, Mayo Clinic has never put money first, instead living its primary value: The needs of the patient come first."[3]

- Steam sterilization rooms, metal surgical tools, knee operated sinks.
- First hospital-based blood bank
- Mayo-Gibbon heart-lung machine
- 1st FDA-approved hip replacement
- Integrated medical record systems
- Use of frozen tissue in cancer surgery
- Nobel Prizes for cortisone
- Regenerative medicine to heal heart tissue
- Rapid DNA testing

1860s
Dr. Mayo places an ad in the local newspaper: opening a practice over a drug store with "all calls answered by day or night."

1880s
Dr. Mayo's sons Will and Charlie join his practice

1890s
Specialization in medicine and railroads, automobiles, and mass communications allows the Mayo Clinic to make its greatest contribution to medicine: integrated multispecialty practice.

1919
The Mayo brothers donate the assets of their practice (land, buildings, equipment, most of their savings) to create a not-for-profit organization dedicated to integrated patient care, medical education, and medical research.

2008
Mayo Center for Innovation founded

2016-2020
Mayo ranked #1 hospital in the U.S. (U.S. News & World Report)[3]

"All calls answered, by day or night" → **Integrated, multispecialty practice** → **Care, education & research** → MAYO CLINIC → **#1 U.S. hospital[3]**

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1. Mayoclinic.org, 2021.
2. Wikipedia: Mayo Clinic, 2021.
3. +Mass Device. Why the Mayo Clinic is a Model for Healthcare Report. 2009.

The Mayo Clinic today

A national model for healthcare reform

"Rochester, Minnesota, where the Mayo Clinic dominates the scene, has fantastically high levels of technological capability and quality, but its Medicare spending is in the lowest fifteen per cent of the country — $6,688 per enrollee in 2006." Atul Gawande, MD[1]

President Barack Obama called Mayo "a national model for healthcare reform."[2] Here's why:

- **Mayo doctors are on salary**. No doctor earns more by ordering an extra test or procedure.
- **Focus on patients, not tests**. Mayo takes a multi-disciplinary approach to care that focuses on symptoms, not tests.
- **Team approach**. Medical care in America is highly fragmented, impeding both efficiency and effectiveness. Mayo attributes the quality of its care to collaboration between specialists.[3]

"Working in an organizational culture that demands teamwork and using such tools as electronic medical records and a sophisticated communication system, Mayo clinicians collaborate to provide the specific expertise needed by the individual patient."[3]

Mayo is the largest private, integrated group practice of medicine in the world, with more than 6,200 physicians, scientists, residents, fellows and students in every medical specialty.[4] Mayo is also Minnesota's largest employer (44,700)[5]

A global hotspot for research

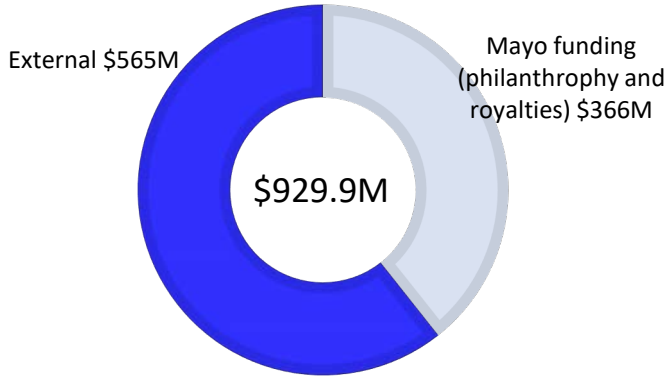
The $5.6 billion Destination Medical Center (DMC) in Rochester, a 20-year economic initiative lead by Mayo.[4]

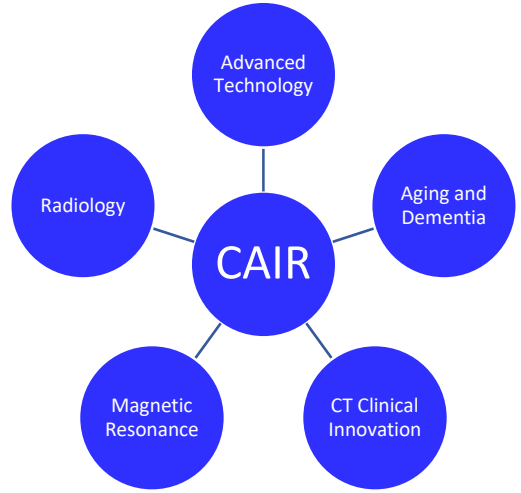
Research personnel: 4,270
Physicians involved in research: 787
Scientific faculty (career scientists): 271
Core research laboratories: 22

Mayo's Center for Advanced Imaging Research (CAIR) at the DMC has five affiliated research centers (right). CAIR brings together clinicians and scientists from across the Mayo landscape for collaborations.

Mayo's center for radiology research offers a fellowship in **artificial intelligence.**

Mayo Clinical research funding in 2020 ($M)[6]





1. New Yorker magazine, May 2009
2. ABC News, Sept. 9, 2009
3. +Mass Device. Two reasons the Mayo Clinic is a model for healthcare reform. July 2009.
4. Mayo Clinic. About Mayo Clinic Ventures. http://ventures.mayoclinic.org/about.php
5. Minneapolis-St. Paul Business Journal, 2020)
6. Mayo Clinic, Research Facts and Funding, 2021

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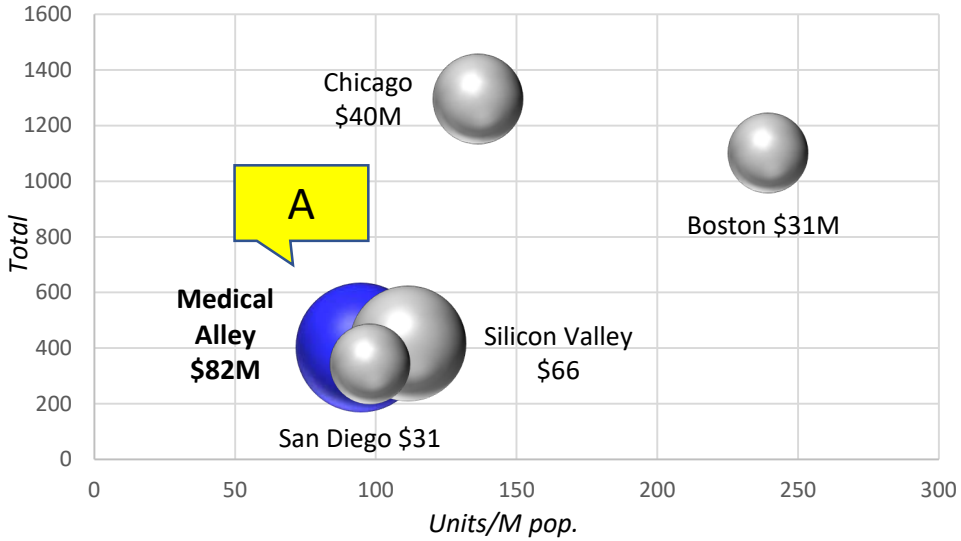
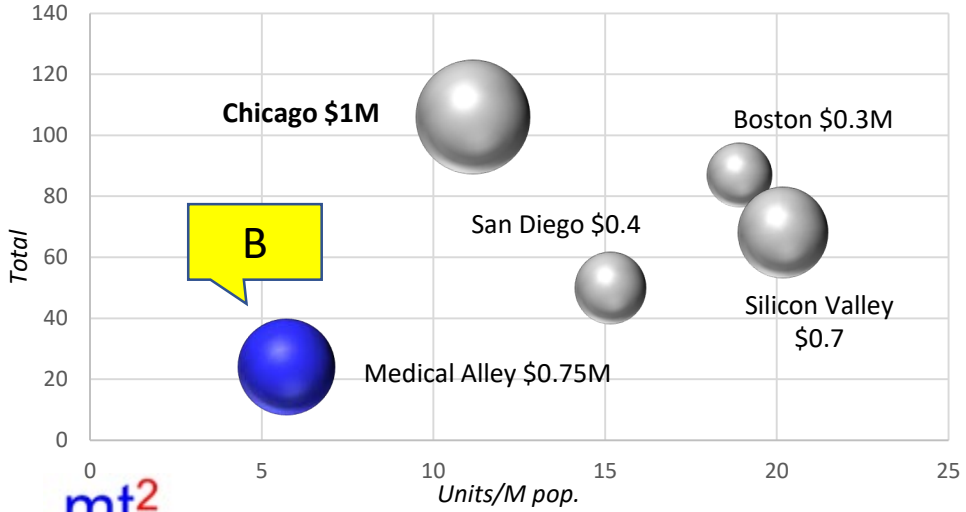
The Mayo influence on Minnesota: high-quality, hospital-based care

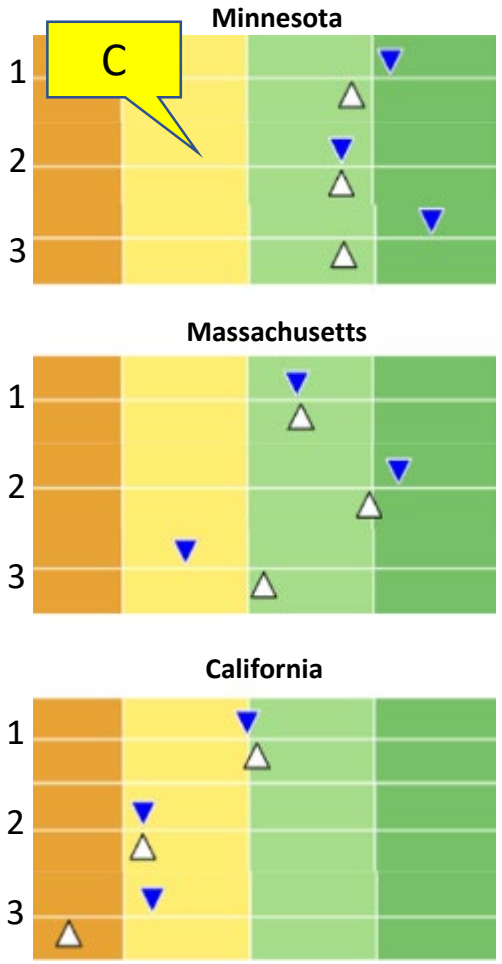
General and surgical hospitals[1] (sized av. unit income)



Ambulatory Surgical Centers[2] (sized by av. Unit income)



Healthcare benchmarks[3]*



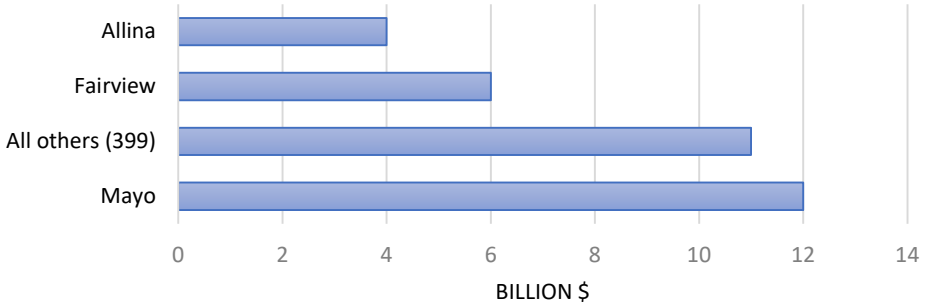
1. Overall effectiveness of treatment
2. Ambulatory care
3. Hospital care

*Marks indicate change from baseline year (white) to most recent year (blue)

Hospital-driven care. Medical Alley (Mpls/St. Paul + Rochester) hospitals have substantially higher patient volumes (as assessed by income) than other benchmark sectors (A), driven by the Mayo, Fairview, and Allina networks (below[1]). Minnesotans tend to be treated in a smaller number of larger hospitals than in other regions.

Fewer ASCs, but cost-effective treatment: Medical Alley fewer patients are treated in fewer ambulatory care centers relative to other regions, though these centers tend to be high-volume (B). To lower costs, the national U.S. payer system (CMS) is incentivizing care conducted outside hospitals. Still, Minnesota delivers high-quality care at a 9% lower per-capita cost than Massachusetts,[4] driven by Mayo's cost-effective care model.[5]

Bottom line: the healthcare delivered by Medical Alley providers is highly effective in both the ambulatory and hospital settings (C).



1 NAICS code 62211; Mergent Intellect database
2 NAICS code 621493, Margent Intellect database
3 Agency for Healthcare Research and Quality, 2021.
4 World Population Review, 2021
5 +MassDevice. Two Reasons the Mayo Clinic is a Model for Healthcare Reform. 2009.

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Minnesota’s medtech heavyweights

Medtronic is moving quickly to acquire and integrate AI

Medtronic
Cardiovascular, surgical, diabetes, neurological, spinal devices

(in millions)		FY20
Cardiac & Vascular Group	$	**10,468**
Cardiac Rhythm & Heart Failure		5,141
Coronary & Structural Heart		3,541
Aortic, Peripheral, & Venous		1,786
Minimally Invasive Therapies Group		**8,352**
Surgical Innovations		5,513
Respiratory, Gastrointestinal, & Renal		2,839
Restorative Therapies Group[2]		**7,725**
Brain Therapies		2,922
Spine		2,503
Specialty Therapies		1,193
Pain Therapies		1,107
Diabetes Group		**2,368**
TOTAL	$	**28,913**

AI is central to 1 of 4 Medtronic's top strategic aims
"Turning data, artificial intelligence and automation into action: In pursuit of efficiency and better outcomes for our customers and patients, we'll apply intelligent data, AI, and automation to tailor therapies in real-time, facilitating remote monitoring and care delivery that conveniently manages conditions."[1]

2020 acquisitions	
Digital Surgery	A U.K. privately-held pioneer in surgical artificial intelligence (AI), data and analytics, and digital education and training. Digitizes surgical protocols to reduce unwarranted variability in surgery.
Medicrea	French artificial intelligence company specializing in using AI for surgical planning. Technology employs predictive modeling and algorithms to measure and digitally reconstruct a patient's spine.
Companion Medical	The only U.S. FDA-cleared smart insulin pen system paired with an integrated diabetes management app.

"We will finally apply computing and AI to surgery on a meaningful scale."[2]

"We are positioning Medtronic to lead in data and analytics – the next big frontier in surgery."[3]

AI means market expansion. Another of Medtronic's top 4 strategic aims is expanding sales into emerging markets, which the company believes are underpenetrated. AI fits with their strategy of "helping more patients in more places benefit from consistently high-quality surgical care."[2]

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Medical imaging *Clinical diagnostics* *Robotics* *AI* ***Key strategic focus***

1. Medtronic 2020 Annual Report
2. Feb. 13, 2020 press release
3. Nov. 16, 2020 press release

Medtronic: recent moves in AI integration

April 12, 2021. FDA Authorizes Marketing of First Device that Uses AI to Help Detect Potential Signs of Colon Cancer.[1]

Medtronic's GI Genius, the first device that uses AI based on machine learning to assist clinicians in detecting lesions (such as polyps or suspected tumors) in the colon in real time during a colonoscopy.

March 22, 2021. Medtronic Receives CE Mark Approval for SenSight™ Directional Lead System for DBS [deep brain stimulation] Therapy.[1]

First-of-its-Kind Directional Lead Combines the Benefits of Directionality with the Power of Sensing. "This is the only directional lead with built-in sensing capabilities," said Jens Volkmann, M.D., Ph.D.

March 17, 2021. Medtronic Receives Approval for U.S. Labeling of the Intellis™ Platform Showing Superior Back Pain Relief When Using DTM™ Spinal Cord Stimulation.[1]

World's smallest implantable neurostimulator...features SureScan™ MRI technology, allowing access to MRI anywhere in the body… AdaptiveStim™ technology automatically adjusts stimulation based on the patient's needs and preferences in different body positions.

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1. Medtronic investor relations

Medtronic is fighting for global leadership in surgical robotics

Medtronic
Cardiovascular, surgical, diabetes, neurological, spinal devices

(in millions)		FY20
Cardiac & Vascular Group	$	10,468
Cardiac Rhythm & Heart Failure		5,141
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TOTAL	$	28,913

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In 2018, Medtronic acquired Mazor Robotics, a pioneer in the field of robotic guidance systems, for $1.6B.[1]

The acquisition strengthened Medtronic's position as a global leader in enabling technologies for **spine surgery.** The company now offers a fully-integrated procedural solution for surgical planning, execution, and confirmation that combines spine implants, navigation, and intra-operative imaging technology with Mazor's robotic-assisted surgery systems (right).

Other Medtronic surgical robotics systems include:

- **Spinal, sinus, and orthopedic** procedures using the S8 Navigation System and Stealth Autoguide robotic guidance platform, and O-arm Imaging System (right)
- **Neurosurgery** using imaging, navigation, power instruments, nerve monitoring, and Mazor robotic guidance systems.

Opening market. Medtronic sees AI and robotics as two parts of the same strategy of automating surgery to open new markets, address the projected shortage in global medical practitioners, and drive adoption through evidence-based reductions in complications and improved outcomes. Medtronic has "doubled-down" on its commitment to bringing robotics into more surgical suites around the world.

Medical imaging *Clinical diagnostics* *Robotics* *AI* ***Key strategic focus***

1. Medtronic investor relations

Boston Scientific is investing heavily in AI integration

Boston Scientific
Interventional radiology, cardiology, vascular, neuromodulation, electrophysiology (pacemakers), and more

"At Boston Scientific, we are continuously exploring new applications for AI systems to benefit clinicians and patients. We also collaborate with research organizations and early-stage ventures to identify new potential uses for AI and machine learning."
Warren Wang, President, APAC, Boston Scientific[1]

Jan. 21, 2021. Boston Scientific acquires wearable cardiac sensor maker Preventice Solutions ($1B)[2]

The sensors connect to PatientCare, the company's cloud-based, EHR-integrated monitoring platform that uses artificial intelligence to provide clinical insights for providers.

Jan. 26, 2021. IBM partners with Boston Scientific on AI-powered pain measurement[3]

"We have developed a new method to measure pain. Our team of neuroscientists, data scientists, engineers, linguists, mathematicians, medical device designers, and clinicians has used AI, internet of things and cloud computing to build a new pain-assessment framework."

July 5, 2019. How one medtech company is working on solving the data dilemma[2]

Application of BS HeartLogic algorithm to data from Latitude remote monitoring system gathered from patients with implanted pacemakers and defibrillators to alert providers of potential heart failure "multiple weeks out."

New wearable sensor with iPhone app

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Medical imaging *Clinical diagnostics* *Robotics* *AI* ***Key strategic focus***

1. MobiHealth News, Jan. 2021
2. Boston Scientific investor relations
3. Medical Design & Outsourcing, July, 2019

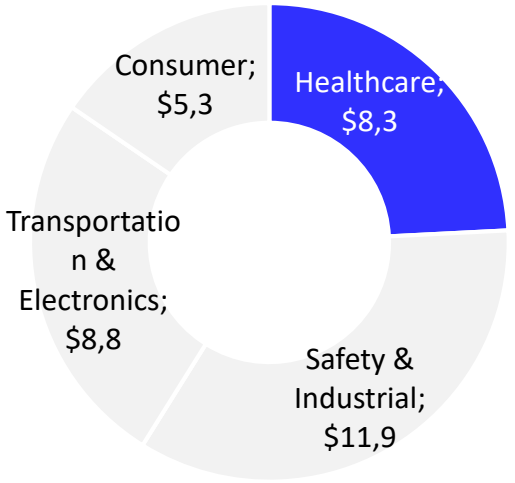
3M Healthcare is investing in AI for patient data handling

3M Healthcare
Surgical safety, infection prevention, patient temp. reg., sterilization and reprocessing, drug-delivery devices and supplies

3M in a nutshell. 3M sells 55,000 products. It specializes in applying core strengths in chemistry, materials science and product engineering to add value to familiar products (e.g., computer screens, inkjet printers, bandaging) across a broad spectrum of industries. After a brief flirtation with high-tech medical technology (e.g., an artificial heart in the 1990s), the 3M Healthcare business returned to the core 3M strategy of adding value to existing, relatively low-tech product categories, e.g., braces, specialized wound dressings and patient warming devices.

What it means. 3M's healthcare division produces the highest margins for 3M.[1] The company is investing in AI to differentiate its healthcare-related software products.

3M total 2020 sales ($B) by business group[1]



In February 2019, 3M acquired M*Modal ($1B), a leading healthcare technology provider of cloudbased, conversational artificial intelligence powered systems that help physicians efficiently capture and improve the patient narrative.

"3M™ M*Modal CDI Engage™ One™ system reduces the administrative burden on physicians and empowers the entire care team to drive better clinical outcomes through advanced artificial intelligence tools. The paperless platform creates a complete and accurate patient story, while allowing physicians to spend more time on patient care and relationship-building."[1]

- Skin, wound care, and infection prevention products
- Dentistry and orthodontia solutions
- Healthcare-related software (EMR, coding, reimbursement)
- Filtration and purification systems
- Food safety indicator solutions

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Medical imaging *Clinical diagnostics* *Robotics* *AI* ***Key strategic focus***

1. 3M investor relations 2021

St. Jude (Abbot): AI and cardiology

St. Jude (Abbot)
Cardiovascular devices and imaging systems, neurostimulation devices

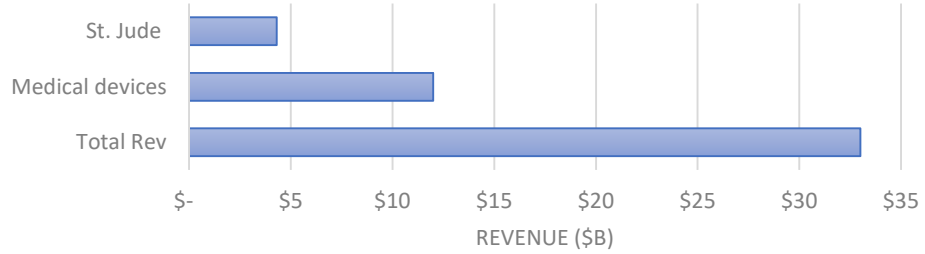
"The American College of Cardiology has partnered with numerous AI companies to develop technologies useful for cardiology."[1]

Sept. 11, 2019. Abbott develops algorithm using AI to help ER doctors detect heart attack

The algorithm is the first created through machine learning to combine high-sensitivity troponin blood testing with other patient details such as age and sex to inform diagnosis

St. Jude in a nutshell. St. Jude Medical has four major clinical focus areas: cardiac rhythm management, atrial fibrillation, cardiovascular and neuromodulation. Their electromechanical portfolio includes implantable cardioverter defibrillators (ICDs), cardiac resynchronization therapy (CRT) devices, pacemakers, remote monitoring systems, cardiac mapping and visualization systems, and neuromodulation devices. Abbott acquired St. Jude in 2016, but the company remains in St. Paul, MN.

St. Jude represents 1/3 of Abbott's medical device business[2]



Electromechanical technologies of special interest:

- OPTIS integrated imaging system: combines fractional flow reserve technology and CT imaging to assess coronary artery disease (CAD).
- MediGuide: a cardiac navigation and visualization technology that enables physicians to locate devices implanted with MediGuide-enabled sensors to reduce radiation exposure during cardiovascular procedures
- Nanostim leadless pacemakers: miniaturized pacemakers implanted in the heart
- CardioMEMS: wireless pulmonary artery pressure (PAP) monitoring technology used to assess cardiac performance

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Medical imaging *Clinical diagnostics* *Robotics* *AI* ***Key strategic focus***

1. Artificial Intelligence Applications in Cardiology. DAIC. Aug. 2020.
2. Forbes, 2019

Expert Opinion

Medical Alley needs in medical imaging, robotics, and clinical diagnostics

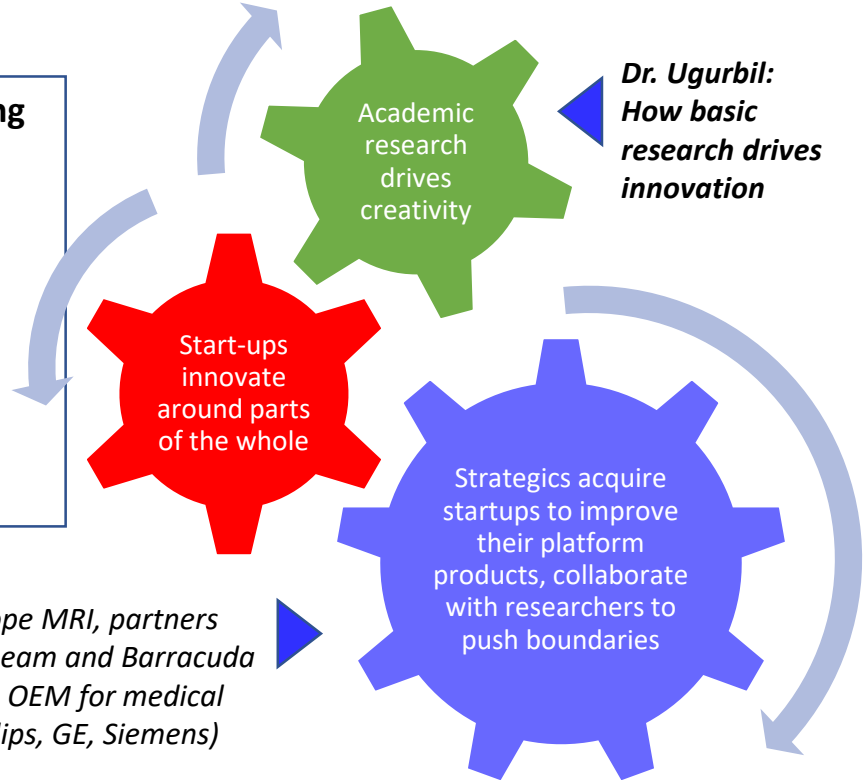
Kamil Ugurbil, PhD: medical imaging

Director, Center for Magnetic Resonance Research, University of Minnesota

- PhD in Chemical Physics, Columbia University, New York
- Currently holds the McKnight Presidential Endowed Chair Professorship in Radiology, Neurosciences, and Medicine at the U of MN

Unmet needs in medical imaging

- Improvement in signal to noise ratios
- Improvement in sensitivity
- Improvement in contrast to differentiate tissue
- AI will make big changes in diagnosis and image reconstruction



Dr. Ugurbil: How basic research drives innovation

Recent example:
Canon Medical acquires Skope MRI, partners with Zebra-Med AI1, Glassbeam and Barracuda to develop their portfolio as OEM for medical imaging strategics (e.g., Phlips, GE, Siemens)

Trends in medical imaging

- Two decades of pushing higher magnetic fields led to introduction of 7 Tesla MRI unit
- Academic research is the “creativity” engine and pushes the boundaries of what is possible for imaging
- Portable ultrasounds improve access to care, speed of diagnosis
- Biggest gains have been in brain and musculoskeletal: targeted, implanted Deep Brain Stimulation possible with higher magnetic field innovations
- Part of the Human Connectome project to map brains using Siemens equipment https: www.ncbi.nlm.nih.gov/pmc/articles/PMC3724347/

Practical advice on engaging with Medical Alley on medical imaging

- Network and conduct many early meetings with anyone that expresses interest
- Dr. Ugurbil singled out Leiden University as a medical imaging knowledge center and overall strength of the Netherlands in AI as Dutch assets that could potentially open doors for engagement in Minnesota

Kamil Ugurbil, PhD: medical imaging

Closer look at unmet needs in medical imaging (Dr. Ugurbil)

Visualization, differentiation and movement. Research initiatives are the driving force in medical imaging, notably in MRI, molecular imaging, and AI integration (particularly image reconstruction improvements). Unmet needs are particularly pronounced in visualization, differentiation, and minimizing or accounting for movement (i.e., improving image quality to see on a smaller scale).

"Any advanced imaging laboratory has to be active in AI."

Single to noise ratios. Innovations to improve signal to noise ratios, sensitivity, and contrast are needed in order to produce earlier, faster, and more accurate diagnoses, particularly in cancer and progressive neuro-disease.

"Disease processes probably take place before anatomy changes…molecular imaging allows you to see the chemistry in the tissue."

Innovation of higher magnetic field devices is needed to improve differentiation and allow for more targeted surgical planning, e.g., implanting deep brain stimulation electrodes where precision matters within 2 millimeters.

"We cannot early-diagnose Alzheimer's but by improving [MI parameters] we could rule out differential diagnoses sooner."

The WU-Minn Human Connectome Project: An Overview

David C. Van Essen[1], **Stephen M. Smith**[2], **Deanna M. Barch**[3], **Timothy E.J. Behrens**[2], **Essa Yacoub**[4], **Kamil Ugurbil**[4], and **for the WU-Minn HCP Consortium**
[1]Department of Anatomy & Neurobiology, Washington University School of Medicine, 660 S. Euclid Avenue, St. Louis, MO 63110, Tel: 314-362-7043; Fax: 314-747-3436, vanessen@wustl.edu

Mapping a new era in brain research. Dr. Ugurbil is a lead investigator in the University of Washington-University of Minnesota Human Connectome Project,[1] which receives funding from the National Institutes of Health (NIH). The Project uses the latest MRI technology to map the brain's connections in ever-greater detail. The creation of a map, or "connectome," is raising hopes that brain disorders like autism and schizophrenia will be better understood in the future--perhaps even cured.[2]

1. Van Essen DC, Smith SM, Barch DM, Behrens TE, Yacoub E, Ugurbil K, Wu-Minn HCP Consortium. The WU-Minn human connectome project: an overview. Neuroimage. 2013;80:62-79.
2. CNN Business. Mapping out a new era in brain research. 2012.

Michael McAlpine, PhD: 3D printing and surgical robotics

Associate Professor of Mechanical Engineering, University of Minnesota

- Ph.D. 2006, Chemistry, Harvard University
- Presidential Early Career Award for Scientists and Engineers
- Kuhrmeyer Family Chair Professor, Mechanical Engineering, University of Minnesota

Unmet needs

- Improved visualization of organ disease
- Broader implementation of soft-printed organ models to aid with surgical planning and training
- Creating robotic systems that are "additive," meaning they can create devices within the body in real time
- Broader use of 3D printed organs to improve patient selection for surgery

"The goal is an all–in-one robotic system capable of surgery AND printing a device directly into the body"

"Current 3D printers use hard plastics and are passive. We want to move towards softer materials and active devices that can be printed directly into or on the body"

Trends and advancements in 3D printing and surgical robotics

- Improved collaboration between strategics, research institutes, and start-ups is the driving force in surgical robotics and 3D printing, particularly in AI integration (e.g., to make printing reactive to its environment), surgical applications, and tactile sensors).
- Microfluidics to allow for at-home diagnostic tools.
- Using robotics and 3D printing applications to customize prosthetics
- Research sponsored by Boston Scientific and Medtronic is aimed at identifying and developing applications for 3D printed soft organ models to aid in visualization of anatomy and provide opportunities for a trials in real-world surgical applications.

"Using tools with the DaVinci system is hard. There is no feedback. Incorporating tactile sensors could be a good thing"

"3D printed organ models can help to minimize complications with better planning"

Practical advice on engaging with Medical Alley

- Tap the brainpower of the U of MN and Mayo Clinic. As of 2017, the U of MN and Mayo combined represented almost $2B in research funding. The U of MN is ranked 17th among U.S. universities in overall funding.
- Take advantage of the collaborative environment in Minnesota. Do not "wall yourself off or try to compete with everyone. It's a collaborative and community-oriented environment"

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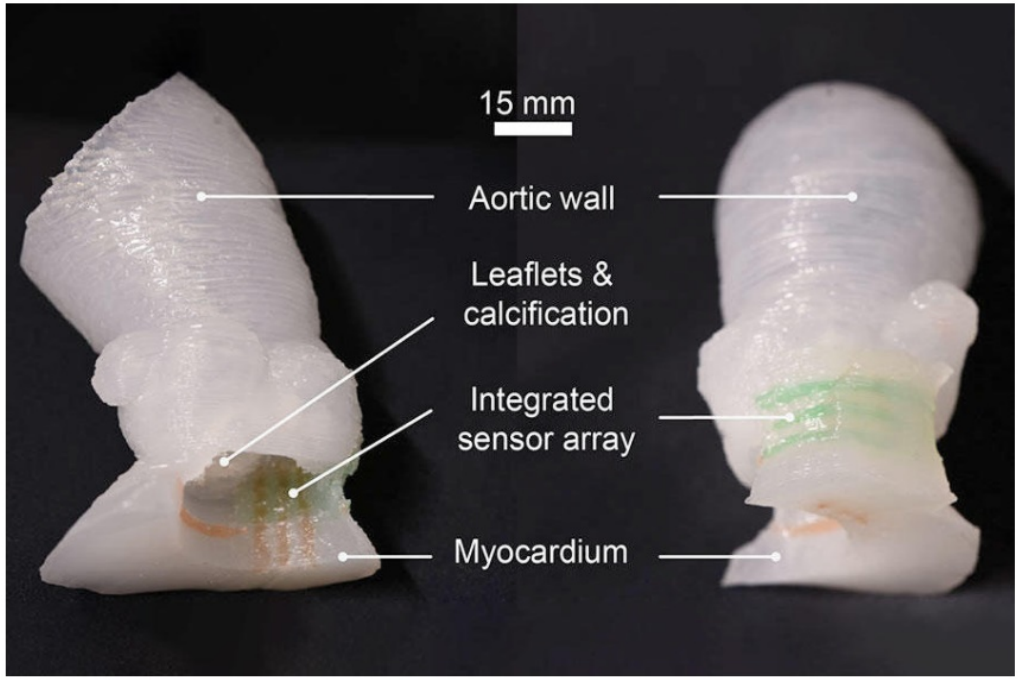
Michael McAlpine, PhD: 3D printing and surgical robotics

3M printing innovations under development at the University of Minnesota[1]

Medtronic is helping to fund research at the University of Minnesota aimed at developing a process for 3D printing of lifelike models of the heart's aortic valve and surrounding structures using a variety of materials to mimic the exact look and feel of an individual's actual tissue.

These organ models, fabricated with special inks and a proprietary 3D printing method, include 3D-printed soft sensor arrays integrated into the structure.

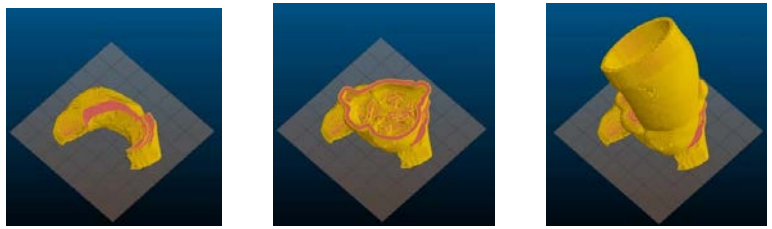
"Our goal with these 3D-printed models is to reduce medical risks and complications by providing patient-specific tools to help doctors understand the exact anatomical structure and mechanical properties of the specific patient's heart," said Michael McAlpine, a University of Minnesota mechanical engineering professor and senior researcher on the study. "Physicians can test and try the valve implants before the actual procedure. The models can also help patients better understand their own anatomy and the procedure itself."



3D printed patient-specific aortic root models with internal sensors for minimally invasive applications [2]

Ghazaleh Haghiashtiani[1,*], Kaiyan Qiu[1,*], Jorge D. Zhingre Sanchez[2,3], Zachary J. Fuenning[1], Priya Nair[4], Sarah E. Ahlberg[4], Paul A. Iaizzo[2,3,5] and Michael C. McAlpine[1,5,†]

3D printing design of the aortic root model with internally integrated sensor array



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1. University of Minnesota. News and Events. Research Brief. Researchers 3D print lifelike heart valve models. Aug. 28, 2020.
2. Haghiashtiani G, Qiu K, Sanchez JD, Fuenning ZJ, Nair P, Ahlberg SE, Iaizzo PA, McAlpine MC. 3D printed patient-specific aortic root models with internal sensors for minimally invasive applications. Science Advances. 2020;6(35):eabb4641.

Bruce Batten, PhD: clinical diagnostics

Founder and CEO, Grip Molecular

- PhD in anatomy & cell biology
- Faculty member at Harvard, Tufts, Ohio State U medical schools
- Ran the MBA program at Augsburg University, Minneapolis
- Founded 4 previous startsups, including Thermo Instruments, CyberOptics and Advantek

GRIP MOLECULAR

"Next generation graphene biosensors enabling lab-quality diagnostics at home."

About Grip Molecular

- Founded in 2019
- GRIP takes a completely different approach to diagnostics by replacing chemical assays with graphene-enabled and dielectrophoresis-enhanced solid-state electronics.
- Users (e.g., patients) will be able to obtain a GRIP panel at a pharmacy, download results to iPhone, and send to a physician prior to teleconference.

Trends in clinical diagnostics (CD)

- **The experiment with lab-on-a-chip (LOAC) has failed** and this technology will not be well-funded in the future. He sees the goal of CD innovation as miniaturizing equipment now found in the central lab. Zepto Life Technology is among the small number of Minnesota startups/SMEs working in the LOAC space.
- **After working to develop LOAC technology himself**, he feels miniaturizing the chemistry-based technology of lab analyzers onto a "credit card" faces major hurdles (e.g., instability, shelf-life, microfluidics) that are unnecessary because of advancements in chemistry-free diagnostics via solid-state technology.

Unmet needs in clinical diagnostics

- CD has focused on identifying pathogens via antibodies. **The new frontier** in CD is the identification of biomarkers of genomic activation (messenger RNA; "micro-RNA") that can flag emerging infection well before antibodies.
- **AI and machine learning** are now being deployed to create "RNA libraries" that would be merged with devices for this purpose. This is an area of opportunity.
- **Mechanical microfluidics enabled by 3D printing** is incorporated into the GRIP device. Microfluidics expertise will be required in future handheld diagnostic tools, regardless of their underlying platform.

Bruce Batten, PhD: clinical diagnostics

"Why should Dutch clinical diagnostics companies care about Minnesota?"

Pros

- **The Mayo Clinic**. Mayo has a "significant business development arm" but "it's the Mayo way or the highway."
- **Progressive medical culture**. Minnesota is "culturally focused on healthcare" and has produced some of the U.S.'s most progressive initiatives in healthcare economics and insurance as well as devices.
- **Strong culture of collaboration** between the University, with its highly regarded medical and engineering researchers, Mayo, and state-sponsored funding for medical innovation.
- **Minnesota's Angel Tax Credit** provides a 25% credit to investors who make equity investments in startup companies focused on high-tech/proprietary technology. The state's "Launch Minnesota" program provides grant funding for area entrepreneurs.
- **3D printing is a regional strength**. The world's leading 3D printing company, Stratasys, has U.S. HQ in Minneapolis. The company is increasing its MDT focus.
- **Quality of life**. Except for the winter climate…this former Bostonian relishes the natural beauty, educated population and way of life in Minnesota.

Cons

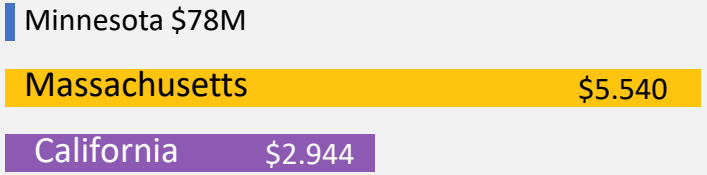
- **"Minnesota is about devices, not biotech."** Minnesota's medtech environment was shaped in large part by Medtronic. In comparison, Boston is much stronger in pharma and biotechnology. However, Dr. Batten routinely collaborates with researchers from the coasts—physical proximity is increasingly less important.

- **Less VC funding than the coasts**. In Dr. Batten's view, startup funding may be easier to acquire in San Diego or the East Coast [as seen in VC funding reports.]

"Mayo is continually trolling for new technologies to explore for collaborations."

"Minnesota is about devices, not biotech."

Income generated biotechnology research and development organizations ($M)*



Practical advice

- Engage with researchers at the U of MN on 3D printing for microfluidics and other applications. Mike McAlpine at the U is "one of the leading global experts" in this area
- Join Medical Alley for connections throughout the Minnesota MDT/HC ecosystem
- Contact the MN Dept of Economic Development (DEED) to explore early-stage funding

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*NAICS 54714, Mergent Intellect database

Perfect matches

Dutch strengths matching Medical Alley needs in device innovation

Opportunities for research collaboration

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Global trends and regional needs driving Medical Alley technology investments

Global trends (accelerated by COVID)

AI and its associated technologies robotics, IoT and 3D printing are being used to improve clinical decisions, reduce variability in diagnosis and surgery, improve device performance, and address projected global shortages in HC providers and expertise.

For the Medical Alley medtech giants, AI will help accelerate expansion into emerging markets, a key strategic focus. AI and its cousins reduce reliance on clinical expertise and enable remote management of devices.

Trends specific to medical imaging and diagnostics[1]

- #1: change in attitude toward acceptance of AI in medical imaging
- Increasing partnerships to expand AI
- Remote access to imaging scanners
- Photon counting detectors as the next major CT innovation
- Point of care – imaging (e.g., ultrasound), diagnostics
- Making MRI easier to use

Unmet needs in medical imaging, clinical diagnostics (KOLs)

Medical imaging

- Improvement in signal to noise ratios
- Improvement in sensitivity
- Improvement in contrast to differentiate tissue
- AI will make big changes in diagnosis and image reconstruction
- Visualization of organ disease

3D printing and robotics

- Surgical planning, and training surgeries via soft printed organ models
- Robotic systems that can create a device *within* the body
- Improved 3D printed organs to improve patient selection for surgery

Clinical diagnostics

- AI and machine learning to create genetic libraries (e.g., RNA) that would be merged with diagnostic devices
- Mechanical microfluidics enabled by 3D printing for future handheld diagnostic tools

State-sponsored funding initiatives are focused on:

- Robotics (1 of 5 focus areas, MNDrive funding)[2]
- Biotechnology and genomics

Medical Alley's medtech giants are now investing heavily in:

- **AI integration into medical devices**
- **AI for surgical planning**
- **Automation of surgical processes, esp. spinal, orthopedic and neuro**
- **AI integration into EMRs**
- **Smart sensor technologies for remote monitoring via wearables**
- **3D printing to enable miniaturization of medical devices (e.g., microfluidics)**

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1. 8 Top Trend Takeaways in Medical Imaging From RSNA 2020. DIAC. 2021
2. University of Minnesota. MN Drive/Robotics. 2021.

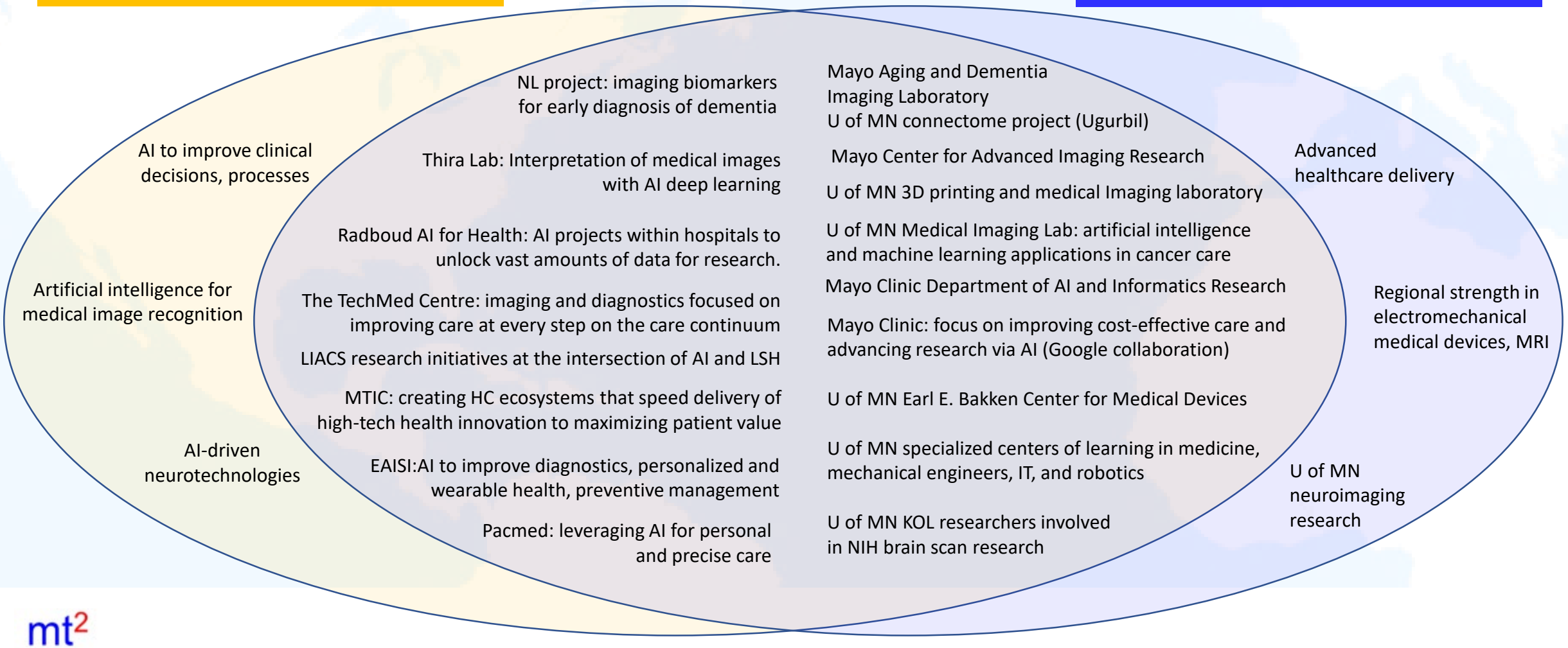
Perfect matches: Medical Alley needs and Dutch strengths

Relevant business divisions	$(B)	AI-related products (examples)	Recent AI-related M&A or partnerships (expression of need)	Dutch strengths
Medtronic	22			Artificial intelligence, materials science, microchip fabrication, and wireless power and communications
Surgical innovations	5.5	• AI-robotics platforms for spine, ortho, neurosurgery	2020 • Digital Surgery • Medicrea • Champion Medical • Ai BioMed	• Machine learning + medical expertise to determine the ideal treatment for individual patients
Respir., GI, renal	2.8	• GI Genius lesion detection		
Brain therapies/stroke (e.g., Deep Brain Stimulation)	2.9	• SenSight directional leads • REVEAL LINQ™ LNQ11 Insertable Cardiac Monitor (for stroke monitoring)	2019 • Klue (AI-enabled analytics)	• BRAIN project: AI in stroke care and management • Neuroscience • AI to improve diagnostics, personalized and wearable health, preventive management.
Spine therapies	2.5	• Intellis platform/AdapStim (nerve stimulation for pain)	2018 • Mazor Robotics ($1.6B) • Nutrino (AI-enabled dietary analytics)	
Diabetes	2.3	• Smart insulin pen		• Machine learning + medical expertise to determine the ideal treatment for individual patients
Boston Scientific	11			Artificial intelligence, materials science, microchip fabrication, and wireless power and communications
Cardiac rhythm	1.7	• Wearable AI-assisted cardiac sensors • HeartLogic heart failure diagnostics • Rhythmia HDX mapping system	2021: Preventice ($1B) 2021: Lumenis global surgical laser business ($1.1B) -	• AI to improve diagnostics, personalized and wearable health, preventive management.
Neuromodulation	0.8			
Endoscopy	1.8			• Imaging and diagnostics focused on improving every point on the care continuum
3M Healthcare	8.3	• 3M AI-assisted EMR, coding and reimbursement support for physicians	2019: M*Modal CDI Engage One system ($1B)	Machine learning + medical expertise to determine the ideal treatment for individual patients • Creating HC ecosystems that speed delivery of high-tech health innovation
St. Jude Medical *Cardiac therapy, monitoring and imaging*	4.3	• Algorithms for early detection of heart attack		• Imaging and diagnostics focused on improving every point on the care continuum

Perfect matches: research and development

The Netherlands
Global leadership at the interface of life sciences and AI

Medical Alley
Global leadership in medical devices and healthcare delivery



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Engaging with Medical Alley

Tim Damgaard Christensen: Engaging with Medical Alley

Program Director, MedTech Bridge

- B.Sc.EE, Electrical Engineering; MBA
- 15 years inhouse product development and project management experience for Danish medtech firms
- Founder & Senior Consultant, Damgaard Christensen Consulting

MedTech Bridge

"We'll help you accelerate U.S. market entry--wisely"

About MedTech Bridge

- Non-profit consultancy funded by the Danish Industry Foundation to help Danish medtech startups and SMEs with U.S. medtech market entry.
- Staff reside in Denmark and Minneapolis
- Close partners with the Medical Alley organization

Why Medical Alley?

- **Cultural similarities**. Danish medtechs (e.g., GN ReSound, Coloplast) have chosen Medical Alley in part because its HC "mindset" is closer to the EU than other U.S. clusters. MN tends to take a more "holistic view" on advancing patient care rather than being driven by the U.S. payer environment.
- **Product development environment**. Silicon Valley's "crash and burn" VC-funded environment is not well-suit to medtech, while Boston is about pharma and biotech
- **The Medical Alley Association** is the foremost organization of its kind in the U.S. and provides access to hundreds of U.S. medtech firms. Minnesota's reliance on medtech also drives state funding.

Practical recommendations

- **U.S. connections are essential**. The most sought-after service Medtech Bridge offers is its "mentor program": MTB finds the ideal U.S. contact for individual Danish MTB members, with a set time allotment (3 X 45 min) and honorarium. MTB organizes customized tours for members.
- **Medical Alley also helps find U.S. hospitals** (sometimes out of state) that help to prove out new medtech solutions.
- **Unique MN medtech resources**. The Earl E. Bakken Medical Device Center at the U of MN offers a two-week "boot camp" on U.S. med device development and commercialization—highly recommended.

Recommended stops on a tour of Medical Alley: University of Minnesota

Medical Imaging

3D PRINTING AND IMAGING LABORATORY, DEPT. OF RADIOLOGY
"An area of active research within the 3DPIL is the use of artificial intelligence and machine learning in cancer therapies [including] use of 3D printing to fabricate patient-specific devices for our patients receiving radiation therapy."

https://med.umn.edu/radiationoncology/research/3dpil
Christopher Wilke MD, PhD
cwilke@umn.edu
Academic offices: 011 612 626 6146

ADVANCED PRECLINICAL IMAGING CENTER (APIC)
"The Advanced Preclinical Imaging Center (APIC) is a state-of-the-art innovative research facility within the Lillehei Heart Institute (LHI) of the University of Minnesota. It serves as a core translational laboratory and training facility to stimulate discovery and advancement in the fields of cardiovascular and neurological science, interventional radiology, and biomedical engineering."
https://med.umn.edu/lhi/research/apic
Phone: 001 612 626 9292
apiclab@umn.edu

Artificial Intelligence

THE VISIBLE HEART® LABORATORIES "are on the forefront of utilizing artificial intelligence to solve problems in the medical field. The focus thus far has been the development of pipelines that utilize convolutional neural networks to automatically segment anatomical features from CT and MRI scans and produce 3D models of said anatomy…Pipelines such as these will likely see use in the future for reducing the time required to develop patient specific 3D anatomical models for surgical planning and post procedure scans for analysis.

"The Visible Heart® Laboratories are also using AI in a variety of ways outside of automatic anatomical segmentation. Other current research topics include developing object detection networks to automatically detect and locate the position of anatomical features within a DICOM scan and using AI to perform point cloud registration between different anatomical models to quickly produce highly accurate statistical shape modeling of anatomical features within a dataset."

"If you would like to coordinate a tour of the Visible Heart Laboratory, contact Monica Mahre at mahre002@umn.edu."
011 612-624-3959

Robotics

MINNESOTA ROBOTICS INSTITUTE
"From surgical robots to self-driving cars, robotics and computer intelligence are changing our lives at a rapid pace. Minnesota is at the frontier of these challenges with global players such as 3M, Medtronic, Mayo, Honeywell, and Cargill looking for creative ideas and human talent." Focus areas:

Medical Robotics and Devices
Faculty Experts: Will Durfee, Suhasa Kodandaramiah, Tim Kowalewski

Artificial Intelligence and Machine Learning
Faculty Experts: Arindam Banerjee, Changyun Choi, Catherine Qi Zhao

Computer Vision and Cognition
Faculty Experts: Changyun Choi, Volkan Isler, Nikolaos Papanikolopoulos, Hyun Soo Park, Catherine Qi Zhao

Manufacturing (Micro and Nano Manufacturing and 3D-printing)
Faculty Experts: Michael McAlpine, Sang-Hyun Oh, Sarah Swisher, Zhi Yang

https://cse.umn.edu/mnri/robotics-research-areas
mnri@umn.edu

Recommended stops on a tour of Medical Alley: Mayo Clinic

Medical imaging

CENTER FOR ADVANCED IMAGING RESEARCH
"Mayo Clinic's Center for Advanced Imaging Research (CAIR) aims to advance the science of imaging techniques, such as MRI and CT, to deliver more accurate diagnostics and a better quality of care. The center brings together clinicians and scientists from across Mayo Clinic in unique collaborations to enhance innovations in medical imaging techniques."

General focus areas:

- Advancement of new MRI acquisition and image reconstruction techniques
- Development of hardware including RF coils, gradients and magnets
- Application of new MRI methods including studies that may have a long-term clinical impact
- Use of MRI to understand disease progression

https://www.mayo.edu/research/centers-programs/center-advanced-imaging-research/contact
Stephen J. Riederer, Ph.D.
011 507 284 9780
riederer@mayo.edu
Diane M. Sauter, R.T.(R)(MR)
011 507 284 4362
sauter.diane@mayo.edu

AI & clinical diagnostics

CENTER FOR INDIVIDUALIZED MEDICINE
"Investigators in the center are using their deep understanding of the disrupted genetics behind disease to develop new approaches to prevent, treat and even cure devastating illnesses — including cancer. First-in-human clinical trials and studies offer life-changing possibilities to families affected by rare genetic diseases. Use of new techniques such as a robust digital platform and new artificial intelligence algorithms is providing hope to those with chronic conditions such as congestive heart failure, major depressive disorder, rheumatoid arthritis and more."

CENTER FOR INDIVIDUALIZED MEDICINE/LABORATORY SERVICES
Services include:

- Genotyping
- Genome analysis core
- Sequencing
- Epigenomics development
- Cytogenics
- Proteomics
- Medical Genome Facility

www.mayo.edu/research/centers-programs/center-individualized-medicine/about/about-the-center
011 507 538 3270

Mayo Clinic – May 17-18, 2021
Artificial Intelligence Symposium – LIVESTREAM

"The Mayo Clinic Artificial Intelligence Symposium aims to bring the health care AI community together to learn about current activities, share best practices, and foster collaborations toward digital health and medicine."

- *Assess the opportunities for artificial intelligence in healthcare for curing and preventing diseases.*
- *Discuss best practices in developing artificial intelligence in healthcare.*
- *Explain how to interpret the privacy, legal, ethics and regulatory challenges faced in advancing artificial intelligence in healthcare.*

May 17-18, 2021
$395

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1. Mayo Clinic. About Mayo Clinic Ventures. http://ventures.mayoclinic.org/about.php

Recommended stops on a tour of Medical Alley: business development

MEDICAL ALLEY ASSOCIATION

"Founded in 1984, the Medical Alley Association [MAA] supports and advances the global leadership of Medical Alley's healthcare industry, and its connectivity around the world. [The MAA] delivers the collective influence, intelligence and interactions that support Medical Alley." The MAA engages with more than 300 ventures each year, offering its assistance in the regional medtech ecosystem while referring companies to high-quality deal flow, connecting companies with other investors, and helping to find strategic advisors. The MAA has hundreds of members throughout the Medical Alley medtech and healthcare ecosystem.

In February 2021, the MAA announced that it launched an accelerator for early-stage healthcare startup companies led by eight entrepreneurs, including Baird Capital partner Nicole Walker and Capita3 founding general partner & managing director Pam York.

www.medicalalley.org
011 952.542.3077
info@medicalalley.org

MAYO CLINIC VENTURES[1]

"To work with Mayo Clinic Ventures is to work with some of the most esteemed medical scientists in the world. The finest minds, focused on a responsibility to make medicine better, collaborate across specialties to solve complex research questions. Such a close integration makes it possible to quickly bring proven diagnostics and therapeutics to patients. Through industry collaborations, Mayo Clinic's innovative technologies are spread worldwide.

"Mayo Clinic research personnel are conducting some 8,000 IRB-approved human studies at any given time. Our scientists publish more than 5,500 research and review articles in peer-reviewed journals each year. An annual research budget of $365 million includes Mayo's own investments in research, philanthropic support, royalties from technology commercialization and external funding."

Mayo Clinic Ventures commercializes novel technologies in biopharma, cardiology, devices, diagnostics, healthcare IT, orthopedics, radiology, and research tools.

011 507 293 3900
mayoclinicventures@mayo.edu

MINNESOTA DEPARTMENT OF EMPLOYMENT AND ECONOMIC DEVELOPMENT (DEED)

One of DEED's strategic objectives is to "make Minnesota's innovation ecosystem a national leader." As such, one of its key strategies is to "increase the number of innovative businesses, organizations, and entrepreneurs we reach with our programs by 25%." DEED focuses on medical device innovation and helps connect entrepreneurs to state-sponsored grant opportunities. Its "Launch Minnesota" initiative covers a broad set of programs aimed at helping high-tech startups grow in the state.

DEED is also an essential resource for companies that seek to establish a presence in Minnesota. DEED can help navigate how to start or locate a business in the state and find staff.

RECRUITMENT
A leading recruitment agency for medtech talent in Medical Alley is Finnesse Partners:
www.finnessepartners.com
info@finnessepartners.com
011 952.232.6170

Methodology and limitations

Methodology and limitations of this report

For calculations of total sales volumes, we used the Mergent Intellect database, a highly flexible web-based application that is integrated with Dunn and Bradstreet's private company database. As this database includes sales numbers for both private and public companies, this approach allowed us to make broad comparisons using NAICS codes, which provide a greater level of detail about a firm's activity than the older SIC-code system. To more accurately capture the kinds of medical device companies we believed our Dutch clients were most interested in, we combined NAICS codes 339112 and 339113, which represent Surgical and Medical Instrument Manufacturing and Surgical Appliance and Supplies Manufacturing, respectively. This meant that certain types of companies that are often classified as medical device companies (e.g., hearing instrument manufacturers, a Medical Alley global strength) were excluded from our assessment. The broadest NAICS code that might be applied to compare medtech clusters may be 3391 (Medical Equipment and Supplies Manufacturing); however, this code includes dental products and laboratories, ophthalmic goods manufacturing, and other products we felt were not relevant for this report.

While the above approach was useful for making broad comparisons, it has limitations. Mergers and acquisitions, which are constant in the medtech space, may skew the extent to which commercial strength or "brainpower" are actually concentrated in one cluster or another. In a few instances, this forced us to make judgments. For example, Medtronic's 2014 acquisition of Covidien—the largest medtech acquisition in history ($42B)—left most of Covidien employees and revenue-generating strength in Boston; therefore, we attributed Covidien's sales numbers to Boston, not Medical Alley. We encountered another limitation in using NAICS codes in the case of 3M, which has a multibillion-dollar healthcare business but has NAICS 327910 (Abrasive Product Manufacturing) as its primary NAICS code. To estimate total sales for the 3M healthcare division, we used the Mergent database to derive total 3M sales and divided these by the percentage of total 3M revenue (via 3M's annual report) represented by the healthcare business. Despite these and other limitations, we felt our methodology was sound for making the kinds of high-level comparisons appropriate to the broad scope of this report.

We used patentsview.org, a patent data visualization and analysis platform, for broad comparisons of the quantity of patents in different regions as an indicator of "brain power" by patient type. This resource is made available by the United States Patent and Trademark Office. This approach has obvious limitations when applied to medical devices. For example, our quick search using the term "medical device" was highly favorable for Medical Alley; however, other reports have credited California with having produced more medical device patents, e.g., 10,061 vs 4268 for Minnesota and 2481 for Massachusetts between 2009-2013.[1] The comparisons used in this report should be interpreted as a general indication of relative medical device know-how in different regions.

Acknowledgements

Valerie Grahn, President and Founder of Grahn MedDevice Consulting, Excelsior, Minnesota, contributed substantially to the design, research, and formatting of this report.

1. Buntz B.. Newmarker C. Top U.S. Medtech States. QMED. Sept. 2015. https://directory.qmed.com/44/resourcefile/05/98/09/Top-US-Medtech-States-1.pdf

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Netherlands Enterprise Agency is part of the ministry of Economic Affairs and Climate Policy.