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CRYONICS

Editorial Board

Saul Kent
Ralph C. Merkle, Ph.D.
Max More, Ph.D.
R. Michael Perry, Ph.D.

Editor

Aschwin de Wolf

Contributing Writers

Michael Benjamin
Max More, Ph.D.
R. Michael Perry, Ph.D.
Aschwin de Wolf

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Address correspondence to:

Cryonics Magazine
7895 East Acoma Drive, Suite 110
Scottsdale, Arizona 85260
Phone: 480.905.1906
Toll free: 877.462.5267
Fax: 480.922.9027

Letters to the Editor welcome:

aschwin@alcor.org

Advertising inquiries:

480.905.1906 x113
advertise@alcor.org
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Since its inception, cryonics advocates have had thoughts of the advantages of like-minded people living in close proximity, or even a community. In particular, a “cryonics retirement community” could make a lot of sense as it allows for faster response and easier logistics, aside from other obvious advantages such as socialization. Mike Perry reviews the history of such attempts with a view towards learning from the past.

3 Getting Better: Part 1: Why do most people believe life is getting worse?

A major obstacle to the growth and success of cryonics is the common conviction that things are getting worse. Since things are getting worse, the future into which we hope to wake will be a horrible place, perhaps nightmarish and apocalyptic. Why would you want to take a journey into such a world? Just how negative are people’s beliefs about progress? Max More shows that: People’s beliefs about the last few decades are highly negative; they are incorrect; and the more uninformed a person is about real trends, the more pessimistic they are about the future.

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The Alcor Case Meta-Analysis project has generated a lot of data to date. Before systematic attempts are made to make sense of it all, the data was organized into a series of basic metrics that permits seeing how Alcor is doing on a number of variables year-to-year. This presentation also includes some further thoughts on implementing the S-MIX to estimate the equivalent-normothermic exposure of a cryonics patient.

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Getting Better

Part 1: Why do most people believe life is getting worse?

By Max More, Ph.D.

We want cryonics to grow for Alcor to grow. Growth means more resources. More resources means more capacity to improve our methods, to fund research, to fight off social, legal, and regulatory attacks, and better prospects for patient revival. For years, membership has been increasing at a single-digit percentage rate. Multiple reasons and factors may help explain this: An unwillingness to believe that cryonics can work; a mistaken understanding of religious doctrines; lack of confidence in one's ability to adapt; lack of enjoyment of life; a belief (true or not) that cryonics is unaffordable; and so on.

A major obstacle to the growth and success of cryonics is the common conviction that things are getting worse. Since things are getting worse, the future into which we hope to wake will be a horrible place, perhaps nightmarish and apocalyptic. Why would you want to take a journey into such a world? Just how negative are people's beliefs about progress? I will show that: People's beliefs about the last few decades are highly negative; they are incorrect; and the more uninformed a person is about real trends, the more pessimistic they are about the future.

Past Golden Ages and Future Ash Ages

In the minds of many, our lives and the world are getting worse and this will continue, so that the future will be worse still. This implies that the past must have been better. Indeed, many cultures include myths of idyllic days of yore. In Western culture, the Arcadian myth conveyed the idea of a past age of pastoralism and harmony with nature. The Garden of Eden embodies some elements of the same idea.

This concept also informed Renaissance mythology. The Golden Age idea similarly saw humans and the world as being corrupted by civilization, production, and rationality (especially in the late 18th to mid-19th century Romantic version in which the past and nature are glorified). The Golden Age as found in Greek mythology describes the decline of the state of peoples through five ages, from Gold to Silver to Bronze and on to the Heroic and Iron ages.

The mythical Golden Age was a time of primordial peace, harmony, stability, and prosperity where perpetually youthful people had no need of work to feed themselves. In South Asia,

related concepts appear in Vedic or ancient Hindu culture which saw history as cyclical, with only one age (Satya Yuga) being the Golden Age. Related ideas appear in the ancient Middle East and throughout the ancient world.

We have been used to hearing about "the good old days." Today, we are more likely to hear this in the form of: "We are destroying the planet and ourselves."

If the past was golden, the future is ash. Popular narratives of the future revolve around violence, starvation, destruction, devastation, hopelessness, slavery, conquerors, dust, and radiation. Let's set aside novels and TV shows and just consider the movies.

The 1950s through the 1970s brought us movies such as *The Day the World Ended* (1955), *On the Beach* (1959), *The Day the Earth Caught Fire* (1961), *Dr. Strangelove* (1964), *Planet of the Apes* (1968) – followed by many more, including *Planet of the Apes* (2001), and *Rise of the Planet of the Apes* (2011), *The Omega Man* (1971), *The Andromeda Strain* (1971), and *Night of the Living Dead* (1968) and *Dawn of the Dead* (1978), *Holocaust 2000/The Chosen* (1977), *Mad Max* (1979) – followed by *Mad Max 2* (1981), *Mad Max: Beyond Thunderdome* (1985), and *Mad Max: Fury Road* (2015), *Soylent Green* (1973), *Zardoz* (1974), *Logan's Run* (1976), and *Damnation Alley* (1977).

The 1980s and '90s thrilled us with *Bladerunner* (1982), *The Day After* (1983), *When the Wind Blows* (1986), *The Terminator* (1984), *Terminator 2: Judgment Day* (1991) and the sequels, *12 Monkeys* (1995), *Day of the Dead* (1985) and its sequels and remakes and all the other zombie movies, *Waterworld* (1995), and *The Matrix* (1999) and its sequels.

The new millennium didn't change our taste for apocalypse and disaster. We were treated to: *World War Z* (2013), *28 Days Later* (2002), *28 Weeks Later* (2007), *The Road* (2009), *Children of Men* (2006), *The Island* (2005), *Snowpiercer* (2013), *The Day After Tomorrow* (2004), *Equilibrium*, (2002), *The Book of Eli* (2010), *Geostorm* (2017), *Cargo* (2017), *How it Ends* (2018), *Mortal Engines* (2018), *Extinction* (2018), and *A Quiet Place* (2018). Most recently, we have seen *Light of my Life* (2019), *I Am Mother* (2019), *IO* (2019), *Songbird* (2020) – a movie about

Covid-23, and *The Covid-19 Pandemic* (2021). Oh, wait, that last one wasn't a movie, it was just surreal.

It's close to impossible to find generally positive portrayals of the future. No wonder so many people reflexively expect the future to be a miserable place they would rather not see.

Mistaken gloom

In his 2017 book, *Progress: Ten Reasons to Look Forward to the Future*, historian of ideas Johan Norberg relates the results of a 2005 study he commissioned looking into the views of 1,000 Swedes on global development. Swedes' answers to eight questions revealed that, in every age and income group, they were wrong on all questions. 73% thought that hunger had increased and 76% that extreme poverty had increased. This was during a period when they had both fallen faster than ever before in history. Disturbingly, those who had been through higher education knew the least about the progress that had been made.

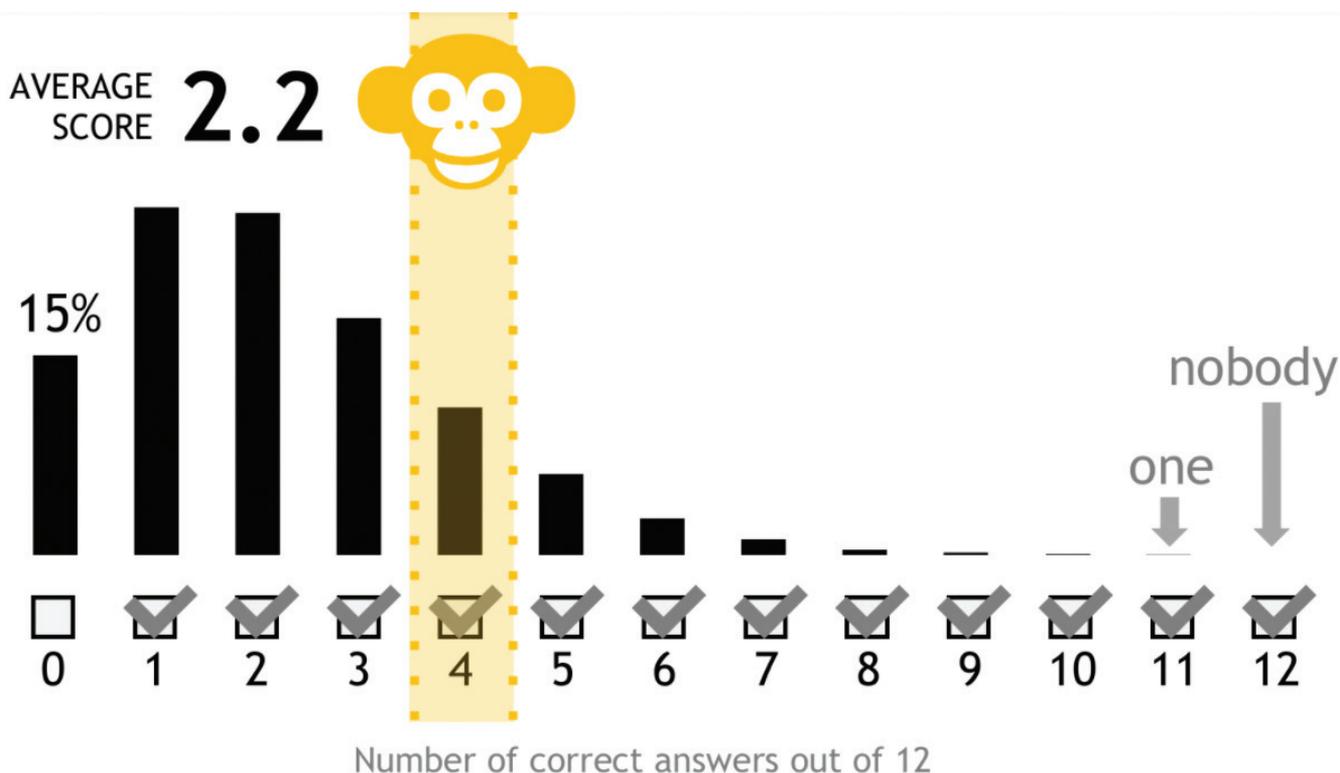
It's not just the Swedes. A YouGov poll conducted in 2015 found that only 5% of Britons thought the world was getting better while 71% said it was getting worse. Respondents in the UK badly underestimated progress in education, health, and fertility reduction in the world. Notably, the results from those with university degrees are not better than the average results. Based on several questions, they are worse. [Norberg, p. 206]

Just a week ago, as I write this, I engaged in a debate at the Oxford Union with some highly educated people. After I had made the case for the desirability of extended longevity, including anticipating objections based on population growth, literature professor N. Katherine Hayles spoke. She reluctantly granted that it might be true that we were polluting less per capita but said she could not imagine that we polluted less in total. If I had been given the opportunity to respond, I would have asked her to step outside and look and smell the air where she was in Los Angeles. Then go and look at pictures of L.A. air a few decades earlier.

More broadly, I would have pointed out that it is not remotely implausible for pollution to fall both relative to population and in total. The population of the USA is growing at around 0.58%. If we can reduce pollution by, say, 0.75% annually, pollution falls absolutely as well as relatively.

In reality, air pollution in major cities has been falling for at least half a century. Soot over Manhattan fell by two-thirds from the end of WWII to the end of the century. In Pittsburgh, Cincinnati, and Detroit, the average number of days of poor air quality fell by around half just in the period from 1978 to 1992. In Los Angeles, the number of days with unhealthy air quality fell by half in one decade, from 1985 to 1995.

According to the US Environmental Protection Agency, between 1980 and 2014 there was a reduction of more than two-



Free teaching materials from www.gapminder.org.

thirds in six major air pollutants: volatile organic compounds, nitrogen dioxide, direct particulate matter, carbon monoxide, sulfur dioxide, and lead. You can see similar trends in the United Kingdom. The concentration of smoke and sulfur dioxide increased in London for 300 years from the late sixteenth century but then fell rapidly. As Bjørn Lomborg put it, “the London air has not been cleaner than today since the Middle Ages.” [Lomborg, 2001.]

In the US and other wealthy countries, water quality has been improving for decades, greatly expanding the number of streams and lakes suitable for fishing and swimming. The number of oil spills has fallen dramatically – by 99% between 1970 and 2014. Deforestation in wealthy countries has stopped and reversed. [Moore & Simon, 2002; Norberg, 2017.]

The Gapminder Foundation has worked mightily to show the gulf between the actual state of the world and its trends and the public’s understanding. The Foundation asked 12 basic fact questions of the general public in 14 wealthy countries. Respondents choose between three alternatives for each question. Purely at random, monkeys could pick 4 out of 12 correct answers. Alas, the score for humans was a sad 2.2.

Since people do much worse than random chance, they must have inaccurate assumptions based on misleading or outdated information. Hans Rosling, professor of international health, discusses these results and the causes in his excellent book, *Factfulness: Ten Reasons We’re Wrong About the World – and Why Things Are Better than You Think*.

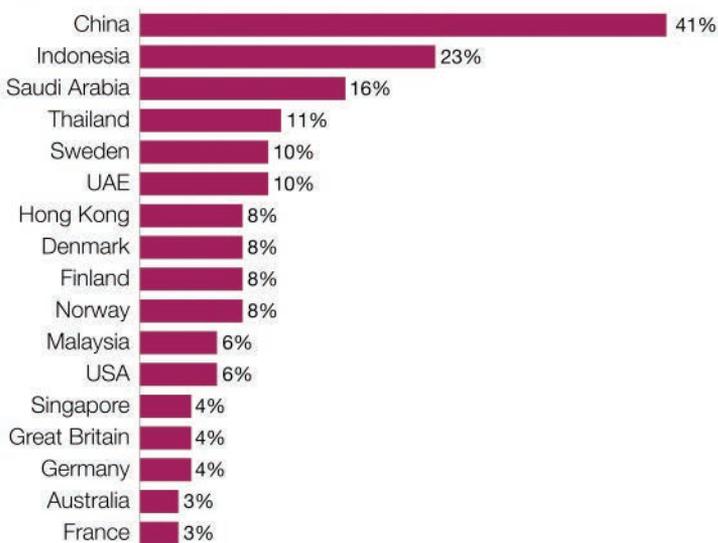
A recent survey asked, “All things considered, do you think the world is getting better or worse, or neither getting better nor worse?” In Sweden 10% thought things are getting better, in the US there were only 6%, and France and Australia were the gloomiest at 4%. The most positive were China at 41% and Indonesia at 23%.

The opinion research organization Ipsos MORI conducted a detailed survey of 26,489 people across 28 countries. [Jackson 2017; Our World in Data ref.1 & 2] The first two charts show that people in every country have falsely negative views of changes in global extreme poverty and in child mortality. 52% believe that the percentage of people in extreme poverty (< \$1.90 per day) is rising. In actuality, this percentage has been declining for two centuries. The reduction in extreme poverty has *accelerated* in the last 20 years.

On the flip side, the number of people who live on over 10 dollars per day increased by 900 million in the last 10 years. This is not to say that everyone is doing just fine. 730 million people are living on less than \$1.90 per day. We can expect that number to still be around 500 million in 2030 since the world’s very poorest economies are stagnating.

The same mismatch between the reality of global progress and subjective, uninformed (or misinformed) belief exists when we consider child mortality. On average only 39% know that the mortality of children is falling. In the USA, only 26% answered correctly, and 34% in Britain. Yet the data clearly show that the “child mortality rate in both the less- and least-developed countries has halved in the last 20 years to 3.9%”. It’s not a

Share of the population who think the world is getting better
 18,235 adults in the following countries were asked “All things considered, do you think the world is getting better or worse, or neither getting better nor worse?”



Data source: Survey conducted and published by YouGov (2015). The is available at OurWorldinData.org. There you find more visualizations on this topic.

Licensed under CC-BY-SA by the author Max Roser.

recent trend. That's a 90% improvement compared to two centuries ago. Again, in this area, progress has accelerated. Here are the percentages dying in the first five years: 1900: 36.2%. 1960: 18.5%. 1990: 9.32%. 2017: 3.9%. Plenty of room for improvement remains since nearly 15,000 children still die per day. [Our World in Data, ref. 2]

When people were asked “over the next 15 years, do you think living conditions for people around the world get better or worse?”, 35% answered “better”, 27% “stay the same”, and 29% “will get worse” (with 9% “do not know”). Japan was the least hopeful (10% better, 44% the same, 26% worse) with France and Belgium the gloomiest (49% worse). The percentage expecting living conditions to improve was 27% in the United States, 25% in Great Britain, and 18% in Germany. Interestingly, the most hopeful were all low-income or lower-middle income countries one generation ago (1990): Kenya (68%), Nigeria (67%), India (65%), China (58%), Indonesia (56%), and Peru (49%).

In 1820 only 10% of people older than 15 years were literate; in 1930 it was one in three and now we are at 86% globally. From a different perspective, in 1800 there were fewer than 100 million literate people of that age; today there are 4.6 billion. When asked about literacy rates today, in the UK, only 8% answered correctly – but only 4% of those with a university education! In the US, 22% answered correctly.

There are “softer” measures of the quality of life in societies that I cannot address here. I will merely quote Andrew Sullivan: “in the midst of tremendous gains for gays, women, and racial minorities, we still insist more than ever that we live in a patriarchal, misogynist, white supremacist, homophobic era.” He also notes: “The more progress we observe, the greater the remaining injustices appear.” [Sullivan 2020].

Those with more optimism about people and the world getting better off in the next 15 years answered more questions correctly. Those who are pessimistic are much less likely to have a sound understanding about what is happening in the world.

When in the past would you prefer to live?

This article (and two more that will follow) contain a lot of information. A better treatment would be the size of a book or three. How can you make a dent in someone’s pessimism when you have only a couple of minutes? The pessimistic answer is: “You can’t! Forget about it.” A more hopeful attitude looks for a shortcut. Here’s what I have often done:

You are talking to someone who clearly thinks the world has gotten worse and will continue down a path of immiseration, environmental destruction, resource depletion, loss of freedom and dignity, and increasing violence. Ask them this question: “When in the past would you prefer to live, compared to today?” Help them out a little. (You can customize your help a bit to fit their sex and race – or their interest in those factors.) Use clear

and vivid examples. Ask them: Would you prefer to live back when:

- There were no painkillers? What if you had to have a tooth pulled or a leg amputated or injured your back?
- There were no antiseptics? If you needed surgery (or what passed for surgery), you would be about as likely to die from infection as from the reason for the operation.
- Women could not own property and had no vote?
- The streets were full of filth, human and animal feces, and rats?
- Slavery was common?
- War was perpetual and conscription universal?
- You would lose most of your children as infants and you/ your wife had a high chance of dying when giving birth?

How has the world changed since you were born?

Here’s a quick, easy, educational, and fun thing to try – and to send to your friends, pessimist or otherwise. Go to this URL to examine “your life in numbers”:

<https://www.humanprogress.org/ylin/>

You’ll find a concise summary of six important ways in which the world has changed for the better over the last 50 years. For instance, globally: Life expectancy has increased from 56 to 72; infant mortality has fallen 72%; average income per person rose 372%, after adjusting for inflation; the food supply increased by 22%; the length of schooling increased 110%; and political freedom rose by 55%.

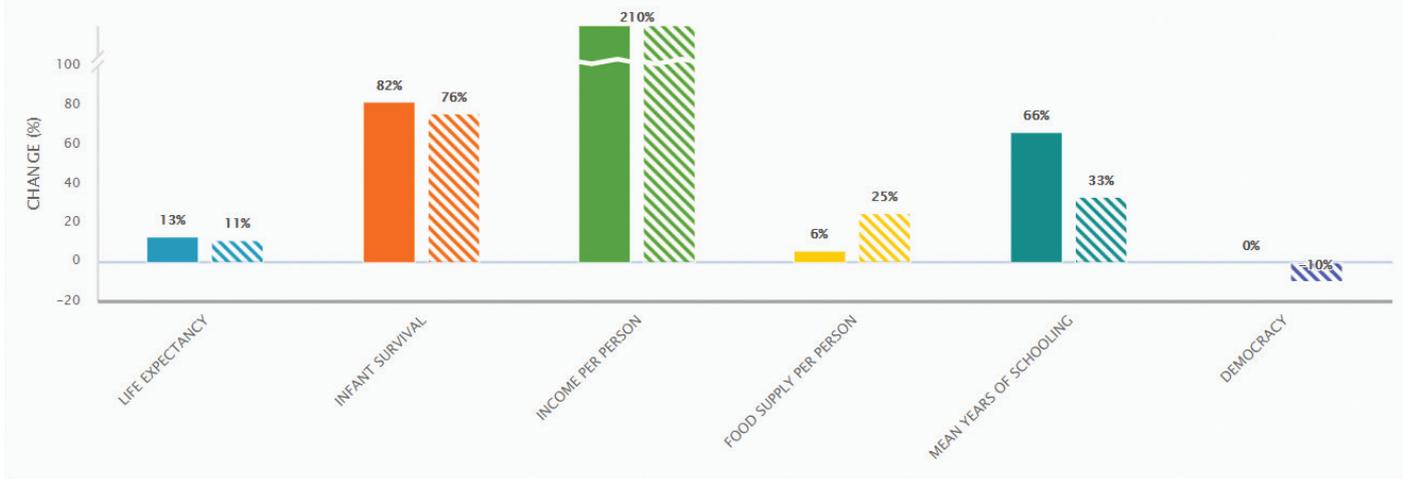
But the fun part comes when you plug in your year and country of birth. Using the massive database at HumanProgress.org, you will then see how your country has changed since you came into existence in terms of the six measures above. You can also plug in another country for comparison. (See graph on page 7.)

This interactive feature only hints at the remarkable depth and breadth of data available on this website. HumanProgress describes itself as “a data-driven educational website devoted to improving the public’s understanding of the state of the world.” Statistics come from reliable third-party sources. You can easily drill down into all kinds of measures of progress. Under “Find Data”, you will find 2259 datasets. You can also dive into the material through around 40 topics. If you like exploring numbers on Worldometer, you will find this absorbing.

Why so gloomy?

What factors strengthen pessimism and unrealistically gloomy beliefs about the present and the future? It’s surely unnecessary

This is how much United Kingdom and United States have changed since 1964



to mention the news factor. More than ever, the working motto of most media is: “If it bleeds, it leads.” The news typically presents us with a tiny selection of the worst events of the last few hours. New stories grab the viewer’s attention by provoking fear with a “teaser.” They want the viewer to stay with them so they suggest that the solution for reducing that fear will be found in the news story. They leave the viewer with more despondency, not less, and wanting more information.

Fear and worry are tools for survival, productions of evolution. In our culture, the context has changed drastically. We are bombarded by negative inputs. And these are bad things that we can usually do little or nothing about. Positive things typically happen over much longer periods of time than negative things. What takes years to build can be destroyed in a moment.

And even without the media distorting our view, our own psychology creates distortion aplenty. The availability heuristic concerns how easy it is to extract something from memory. The more memorable an incident is, the more probable we think it is. Bad news tends to stick in the mind better and is more easily recalled. There is also “the psychology of moralizing.” Complaining and criticizing sends a signal to others that you care about them. “Bad” information usually gets processed more thoroughly than “good” information.

Our tendency toward “declinism” – a predisposition to view the past favorably, and worry that the future is going to be bad – seems to be due to the combination of two factors: the “reminiscence” bump and the positivity effect. The former was identified in studies from the late 1980s and early 1990s. “Researchers showed that when they asked 70-year-olds to recall autobiographical memories, they tended to best remember events that happened to them at around the ages of 10-30. Recall dropped for events that happened when the participants were

aged between 30-60, and then increased again for ages nearer to 70. So, you’re more likely to remember things that happened to you in late childhood or early adulthood.”

The positivity effect is the idea that as people get older, they tend to experience fewer negative emotions, and they’re more likely to remember positive things over negative things. The combination of the reminiscence bump and the positivity effect means that:

people are more likely to remember events from late childhood or early adulthood, and critically more likely to remember positive events from the past. In other words, you remember your younger years more favourably, which might go some way to explaining why some people experience declinism. [Etchells, 2015.]

In this first article in what I expect to be a three-part series, I have shown that most people believe that life is getting worse. I’ve given or pointed to strong evidence that this belief is mistaken. Over time, life is getting better in numerous important ways. And I’ve briefly noted some of the factors shaping our excessively pessimistic beliefs.

In the next article, I will go into more depth on some measures of well-being. These measures cover such things as the environment, equality, education, political freedom, racism, oppression, and non-renewable resources. I plan to cover the Simon-Ehrlich bet and look at the appalling number of bad pessimistic predictions – a record of failure from which we fail to learn.

In the third article, I will consider whether we can expect things to continue to get better. What economic, cultural, and

technological factors may drive further improvements? What political or other factors could threaten progress? And what, if anything, might we reasonably expect of the world into which we hope to one day be revived? ■

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Our World in Data:

1. <https://ourworldindata.org/wrong-about-the-world>
2. <https://ourworldindata.org/a-history-of-global-living-conditions-in-5-charts>

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Alcor Longevity Circle of Distinguished Donors

The Alcor Board of Directors is pleased to announce the formation of the **Alcor Longevity Circle of Distinguished Donors**. This new organization will honor those members and their foundations that have donated in excess of \$100,000 over the past few years to support Alcor and its affiliated organizations. In addition to being recognized in Alcor publications and at conferences and other events, members will also be entitled to:

- Exclusive access and a quarterly conference call with Alcor Directors, officers, and officials to get in-depth briefings and ask questions and make suggestions.
- Special recognition, seating, and access to officials at Alcor conferences.
- An exclusive yearly, hosted in-person event honoring members with face-to-face interaction with Alcor Directors, officers, and officials.
- A unique, professionally designed and engraved memento of their membership.



These benefits are, of course, overshadowed by the immense gratitude members' and patients' families will always have for these especially generous individuals. New levels of membership (higher and lower levels of participation) may also be announced in the future. ■

Support Alcor's **RAPID** Research

Readiness **And** Procedure Innovation/**D**eployment (**RAPID**)

In order to advance the science and reputation of cryonics, Alcor plans to conduct ongoing research to develop novel and near-future products related to cryopreservation procedures and protocols. The RAPID team is developing relationships and contracts to procure recently deceased human cadavers, which are not Alcor members or patients, but are already earmarked for medical research. The idea is to procure one to two cadavers per month to conduct research. We would go on a "light standby" to enable fast access to cadavers.

The RAPID initiative will support cryonics research in multiple ways. Most immediately, it will help advance research into liquid ventilation – using a patient's lungs as a heat exchanger to induce very rapid hypothermia. Animal studies alone cannot take LV development to the next level due to different chest anatomy. LV research will include cooling rate control; chest compression studies; and timing and sensor feedback.

RAPID will also enable research comparing chemical fixation to cryoprotection and will support rewarming studies. Another benefit will be a great improvement in cryonics-specific surgical training. That includes raising and cannulating the carotids; cephalic isolation; raising and cannulating the femoral arteries; field neuro procedure training; median sternotomy training; and alternate surgical approaches.

Alcor is requesting donations through GoFundMe. All donors will receive quarterly reports from Alcor regarding the progress with fundraising and milestone achievements rising from the RAPID program! Please donate today to support Alcor's RAPID initiative. Alcor is a non-profit, federally tax-exempt, 501(c)(3) corporation and your donation may be tax deductible. ■

Donate here: <https://charity.gofundme.com/o/en/campaign/rapid-research/alcorlifeextensionfo>

For more information, see the presentation here: <https://www.youtube.com/watch?v=BUaVcVMuFWQ&feature=youtu.be>

Alcor Case Metrics 2000-2020

By Michael Benjamin and Aschwin de Wolf

Introduction

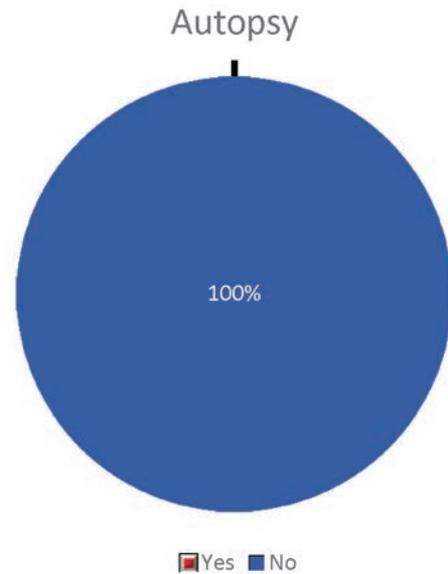
The Alcor Meta-Analysis Project has three distinct objectives: (1) To organize and enter all case data in a comprehensive database; (2) to visually present and publish the data in a format that allows the reader to see trends and patterns; and (3) to identify correlations between specific elements of a case and outcomes.

We present here a selection of case data for the years of 2019 and 2020. This is followed by a more global presentation that covers the period from 2000 to 2020, which roughly coincides with the introduction of vitrification technologies at Alcor.

At this stage in the meta-analysis project, we still confine ourselves to presenting factual data and calculated (or estimated) measures. After completing this project for all Alcor cases, we will move to the next step of identifying trends and correlations.

The magnitude of the project and sheer quantity of data means that some errors are expected in the reporting or interpretation of data. In some cases, detailed data is not available and rough estimates need to be made based on the case data that was available and extrapolation of what we know from other cases. We expect this project to increase in comprehensiveness, accuracy, and actionable information.

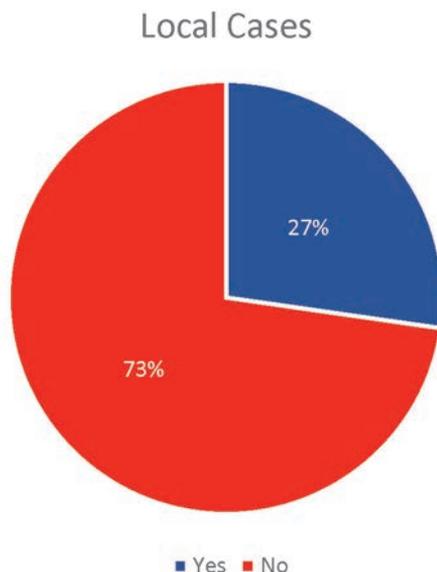
A local case is defined as a case in the greater Scottsdale, Arizona area.



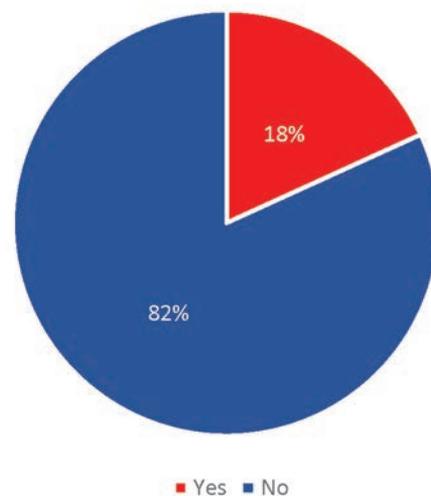
In some circumstances (like sudden death), an autopsy is ordered. Alcor typically objects to prevent an (invasive) autopsy but is not always successful.

2019

There were 11 cases in 2019, 10 Neuro and 1 Whole Body.

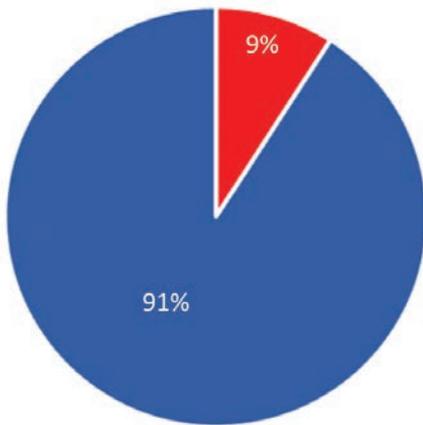


Unattended Deaths



Unattended death cases are cases in which a patient experiences circulatory arrest without medical caregivers or family present. This often happens to older members who live alone.

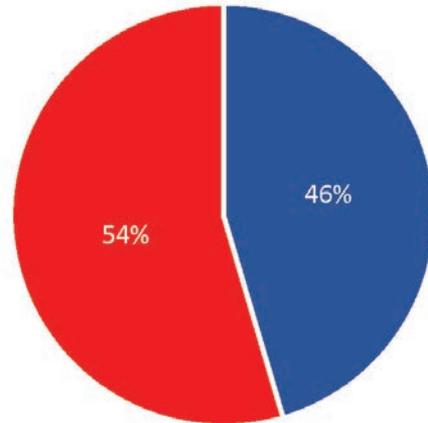
Straight Freeze



■ Yes ■ No

A straight freeze is a case in which a patient is frozen without any kind of cryoprotection to prevent freezing damage. Straight freezing usually happens in case of long ischemic delays, after autopsy, or when there is a delay in arranging for cryonics arrangements.

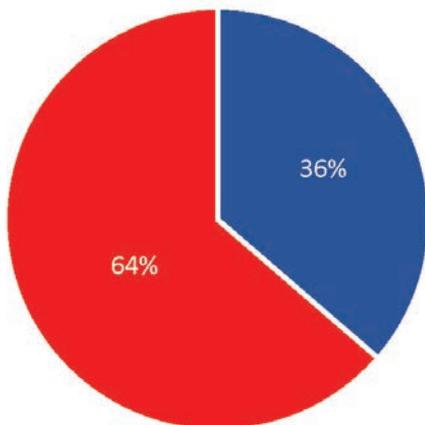
Medications Administered Full Protocol



■ Yes ■ No

This chart refers to cases in which the complete stabilization medications protocol was administered. This is typically associated with pre-mortem standbys.

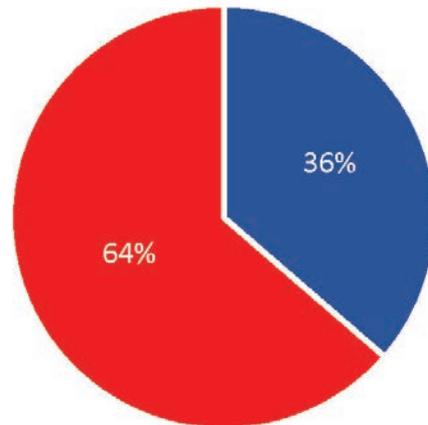
Pre-Mortem Standby



■ Yes ■ No

Pre-mortem standby refers to cases in which a (professional) standby team was deployed to the patient's location before pronouncement of legal death.

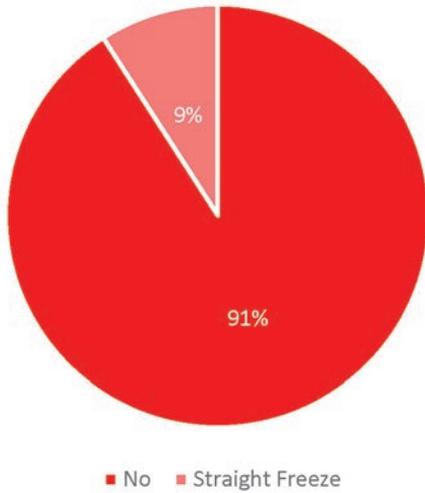
Cardiopulmonary Support (Chest Compressions & Ventilation)



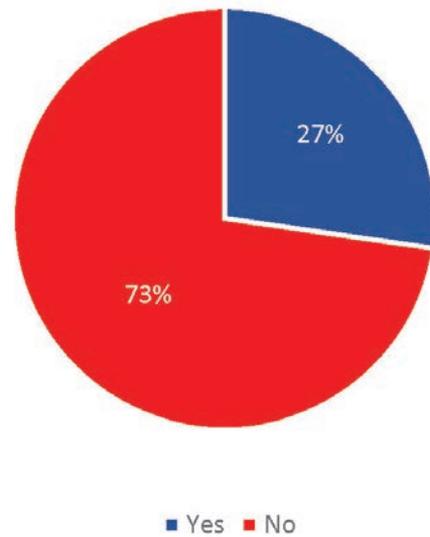
■ Yes ■ No

In the meta-analysis project cardiopulmonary support (CPS) cases are cases in which chest compressions PLUS ventilation is performed on the patient as part of stabilization procedures. Brief periods of chest compressions to circulate medications are not included in this category.

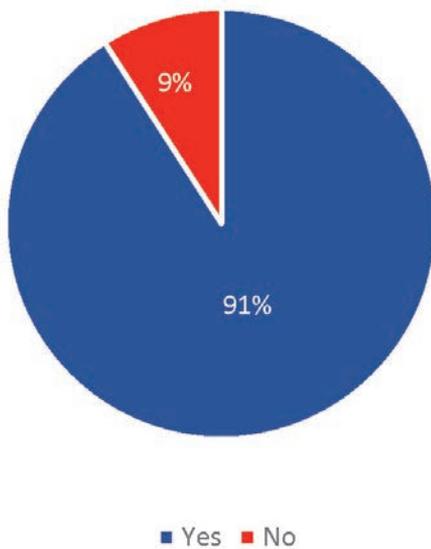
Field Cryoprotection



Terminal Cryoprotection Concentration Achieved

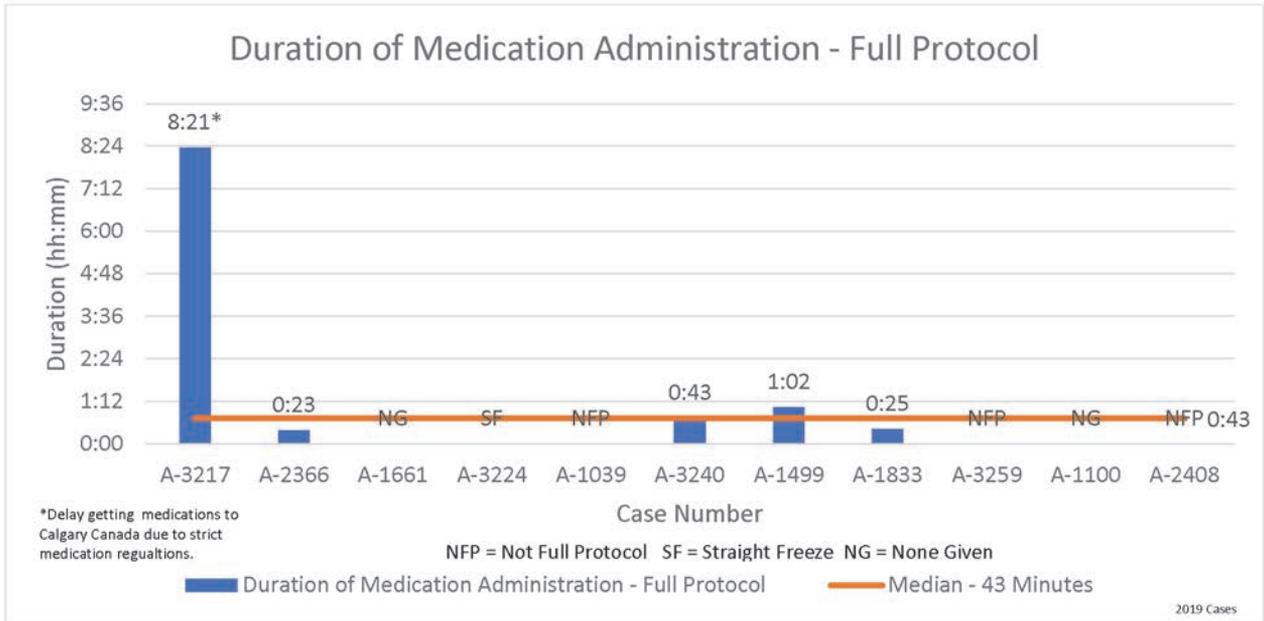


Cryoprotective Perfusion

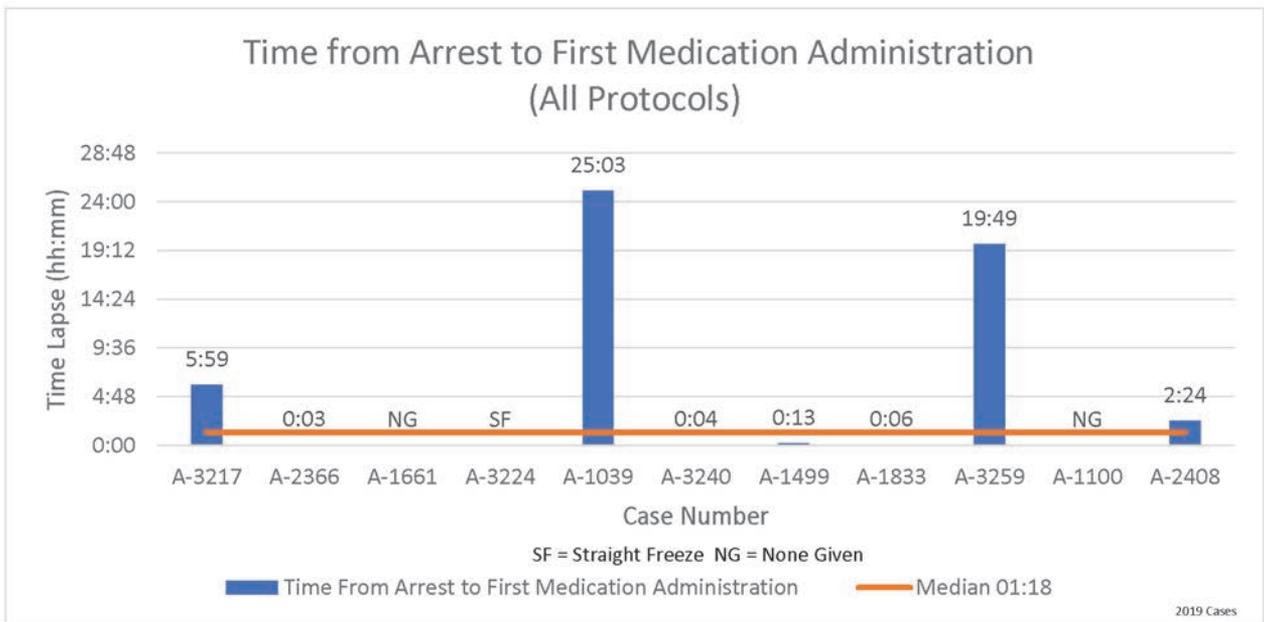


Cases in which the terminal cryoprotection concentration was achieved are cases in which the full concentration deemed necessary for vitrification to occur was obtained. In patients with prolonged ischemic exposure this target is not always achieved.

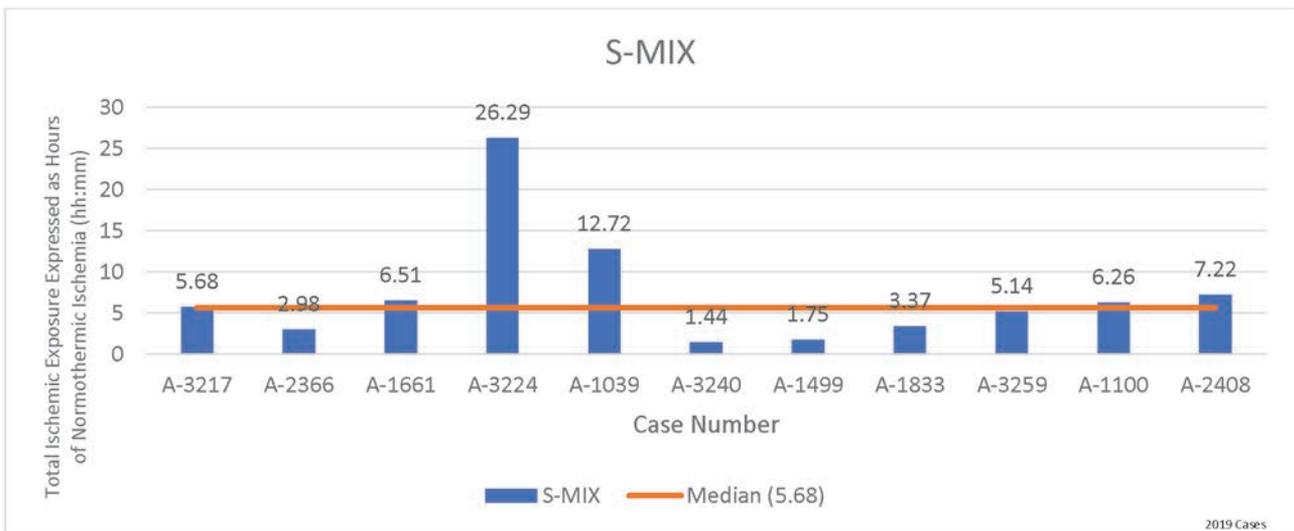
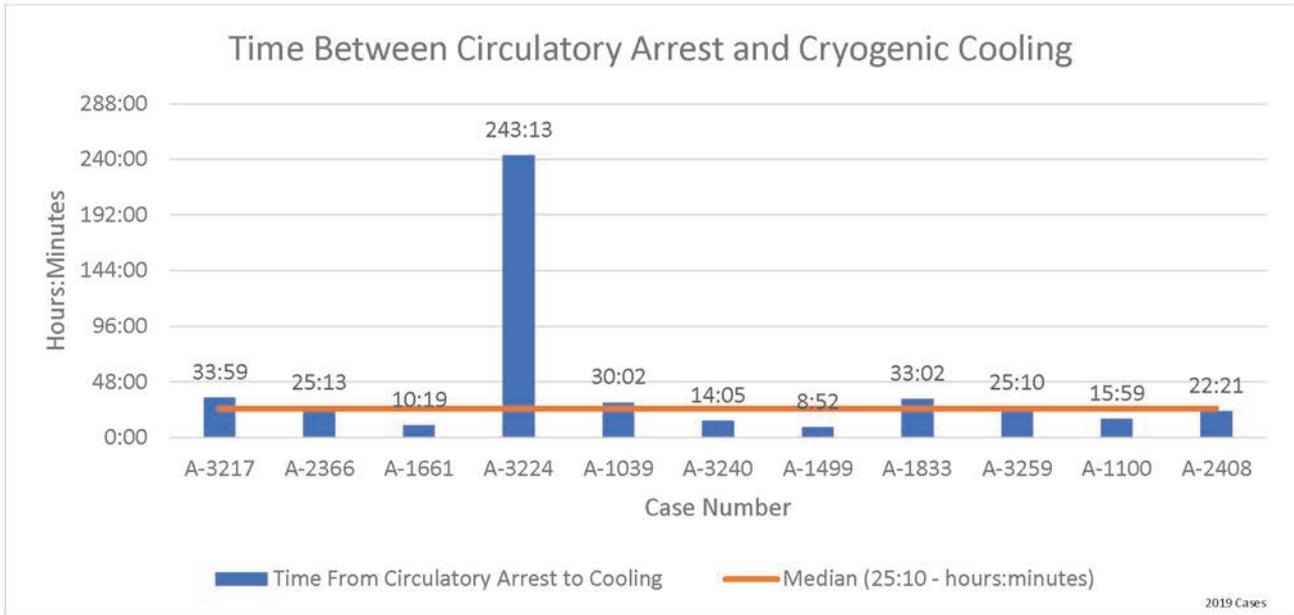
Cryoprotective perfusion cases are cases in which a cryoprotectant was delivered to the patient through perfusion of the blood vessels. As a general rule, when there is no cryoprotective perfusion, the case is a straight freeze.



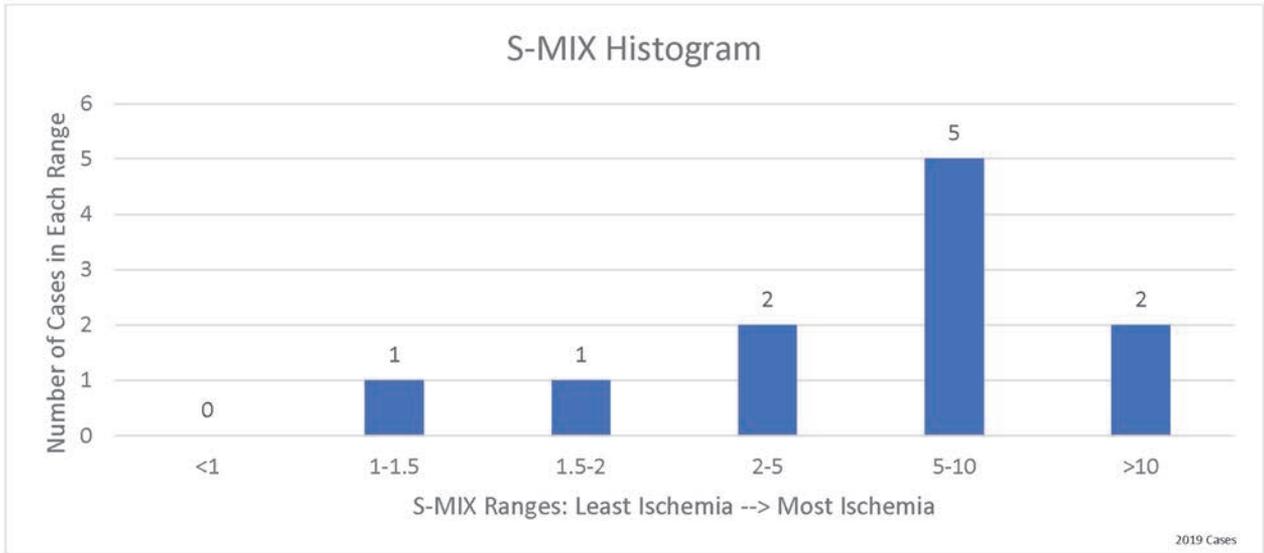
Duration of medication administration refers to the total time it took to administer all the stabilization medications in the full protocol.



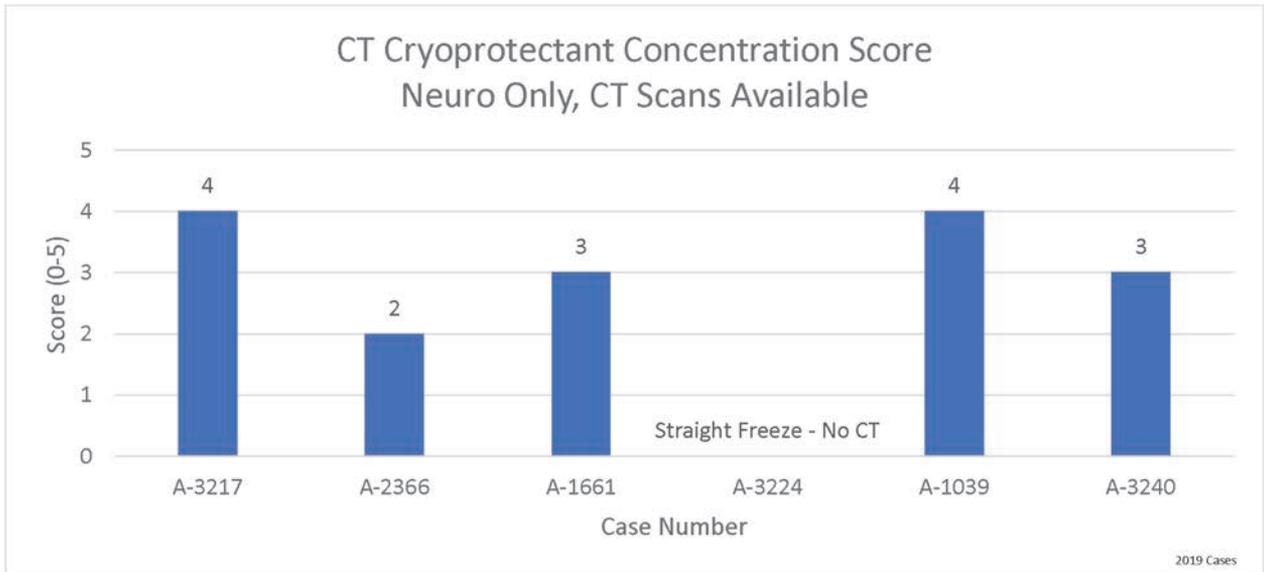
Time from arrest to first medication administration is the time between circulatory arrest and administration of the first medication. This can concern the full protocol, abbreviated protocol, or a single medication (like heparin).



S-MIX stands for **Standardized Measure of Ischemic Exposure** and calculates the total equivalent normothermic ischemic exposure of a patient. The higher the S-MIX, the higher the degree of ischemic exposure of a patient.

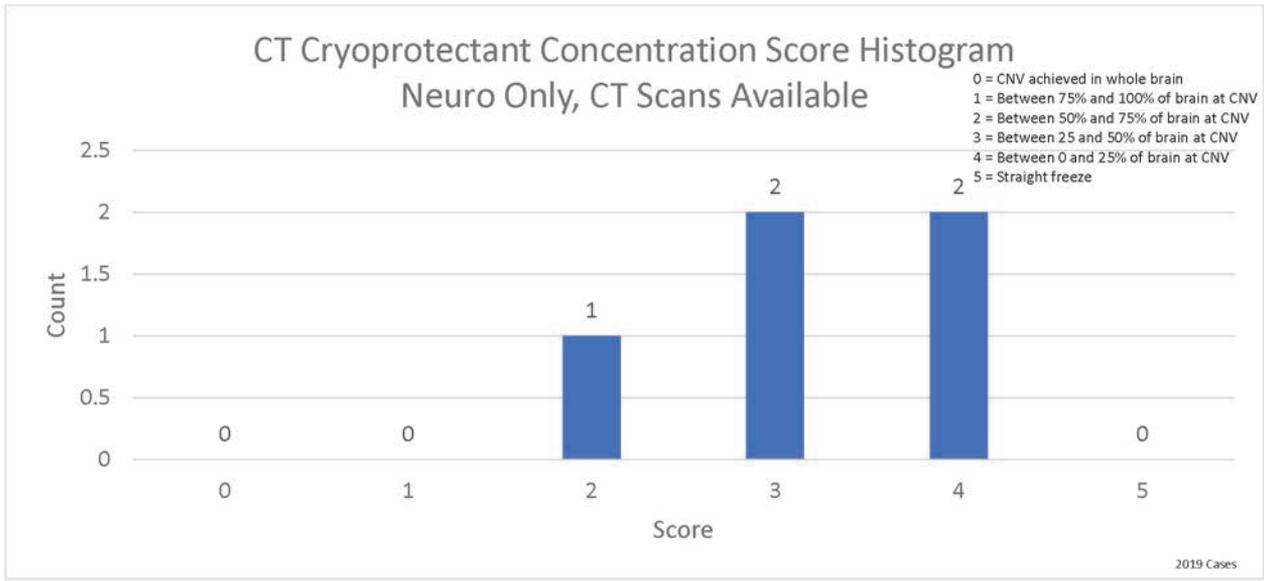


In the S-MIX histograms all cases are divided into 6 different categories ranging from least ischemia to most ischemia.



- 0 = CNV achieved in whole brain
- 1 = Between 75% and 100% of brain at CNV
- 2 = Between 50% and 75% of brain at CNV
- 3 = Between 25 and 50% of brain at CNV
- 4 = Between 0 and 25% of brain at CNV
- 5 = Straight freeze

The CT cryoprotection concentration score is an estimation of the amount of brain area with concentrations of the cryoprotectant to inhibit ice formation.

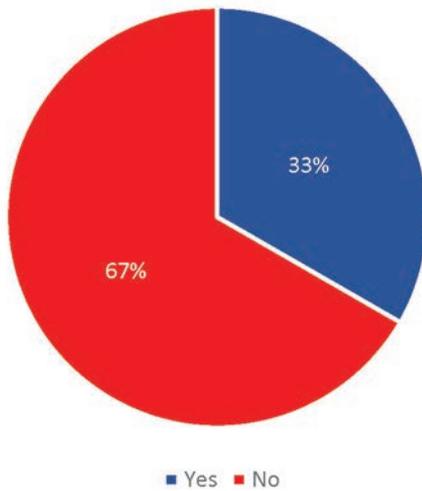


The CT cryoprotection concentration score histogram shows the number of cases in each concentration score.

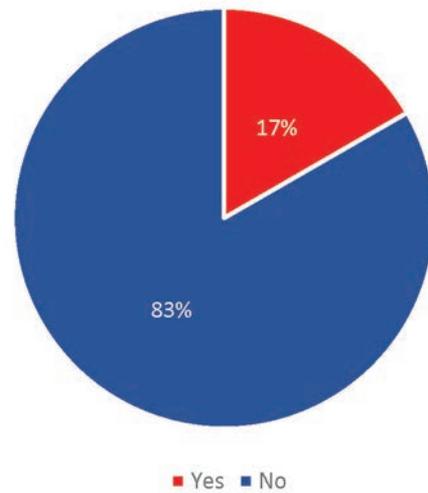
2020

There were 6 cases total in 2020, 4 Neuro and 2 Whole Body.

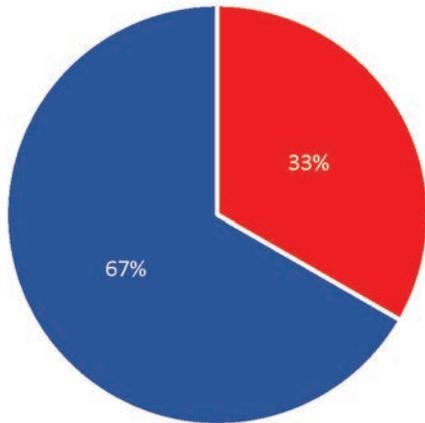
Local Cases



Autopsy

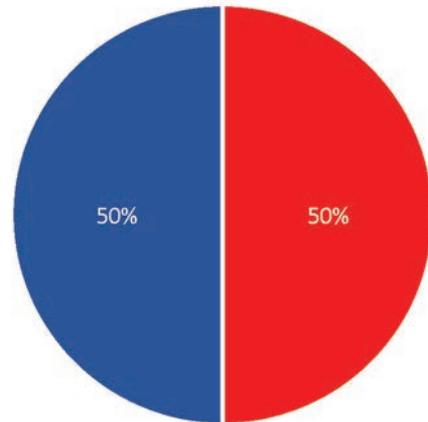


Unattended Deaths



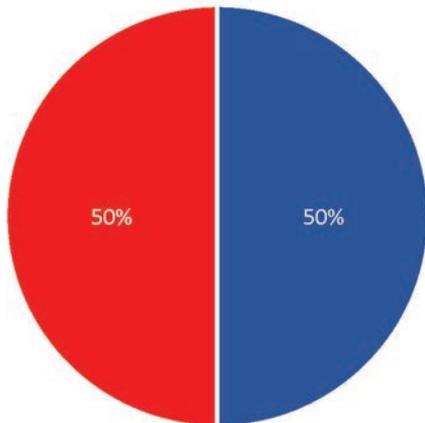
■ Yes ■ No

Straight Freeze



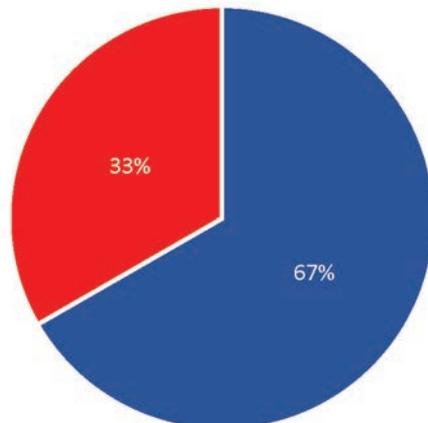
■ Yes ■ No

Pre-Mortem Standby



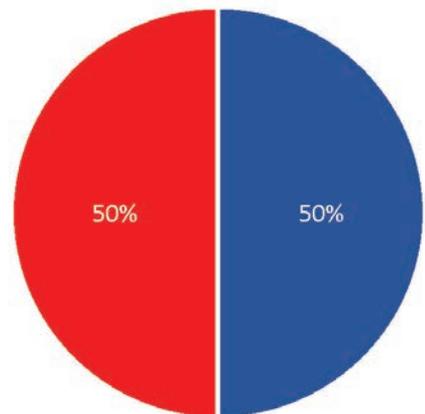
■ Yes ■ No

Medications Administered Full Protocol



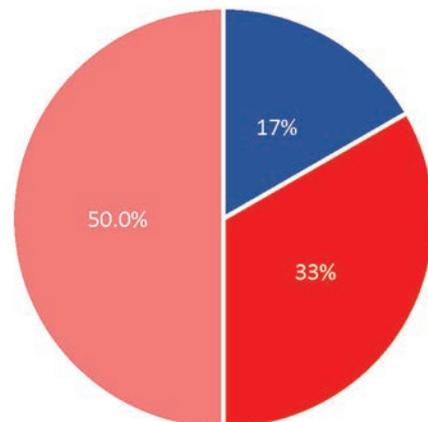
■ Yes ■ No

Cardiopulmonary Support
(Chest Compressions & Ventilation)



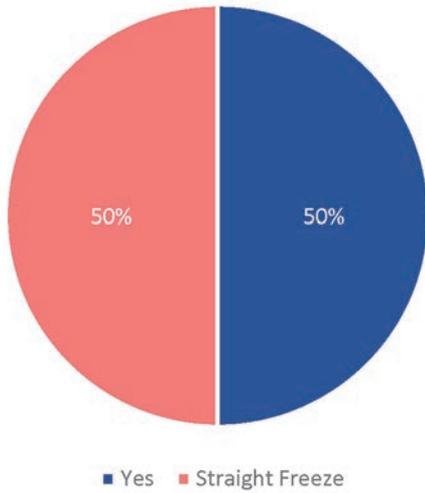
■ Yes ■ Straight Freeze

Field Cryoprotection

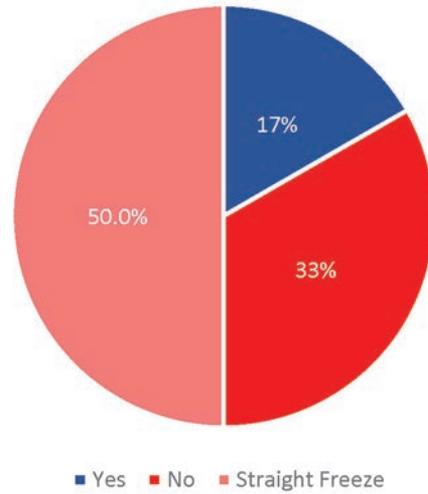


■ Yes ■ No ■ Straight Freeze

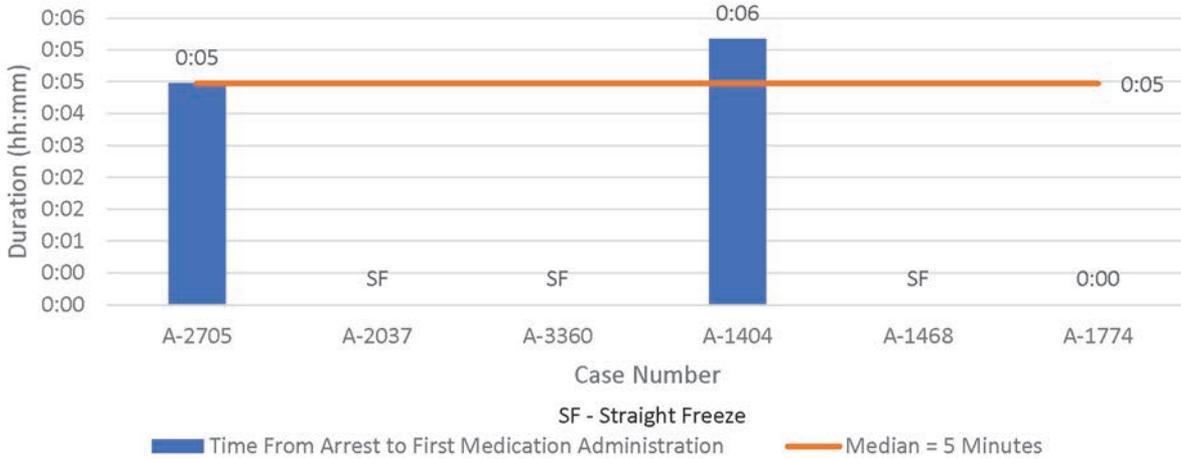
Cryoprotective Perfusion

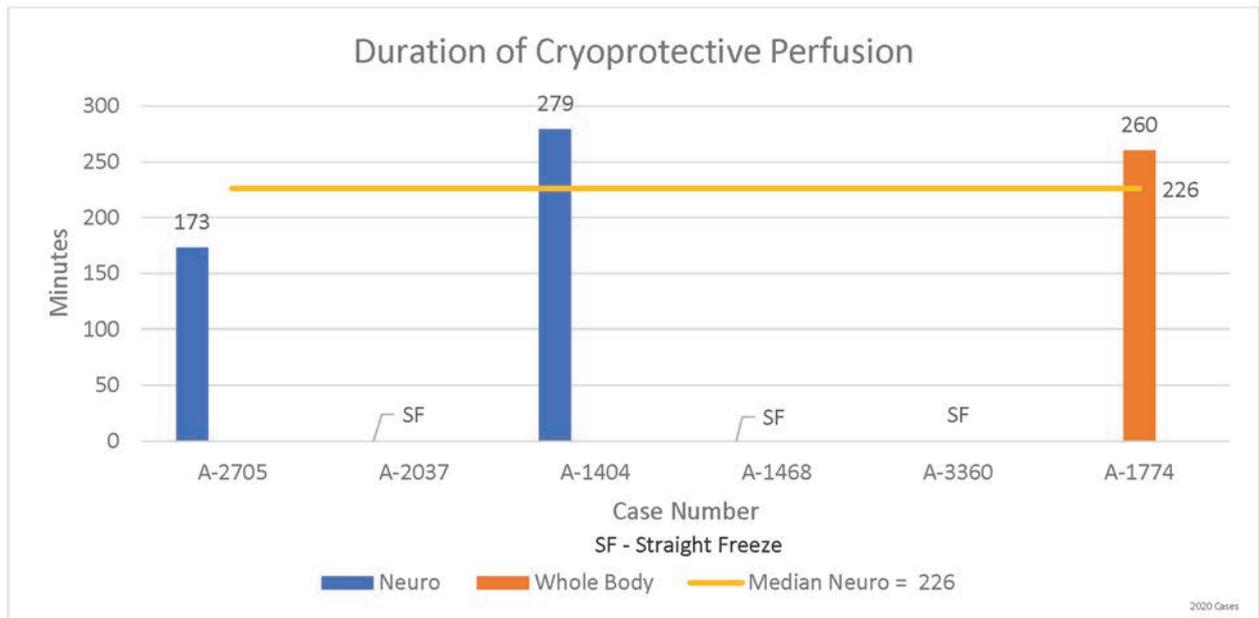
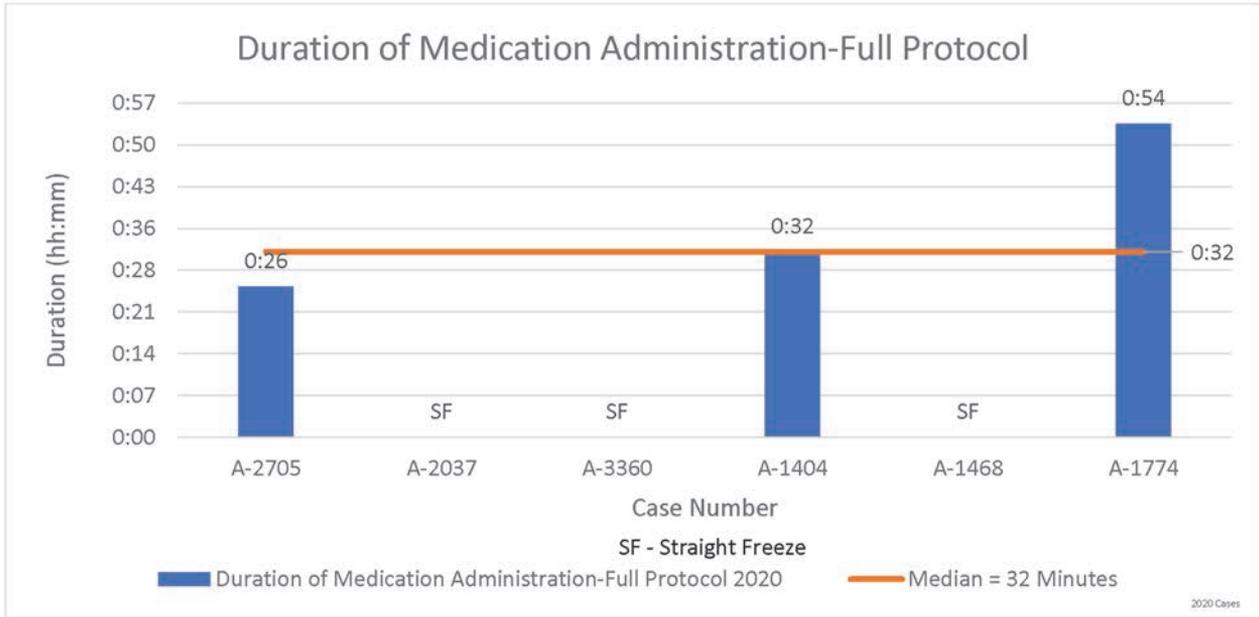


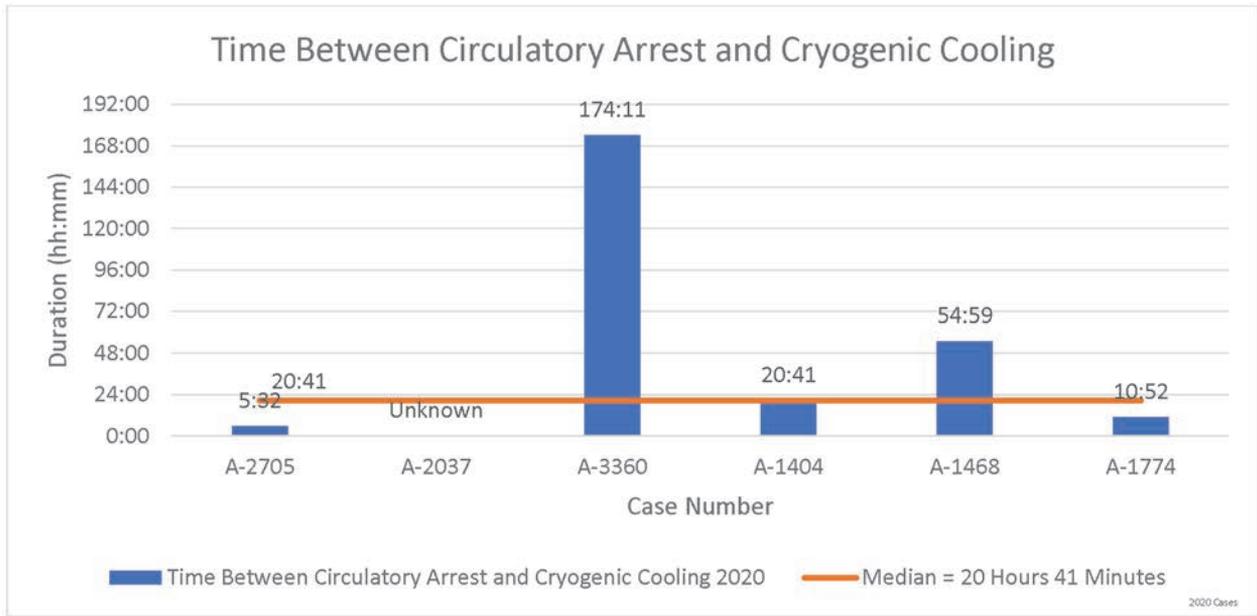
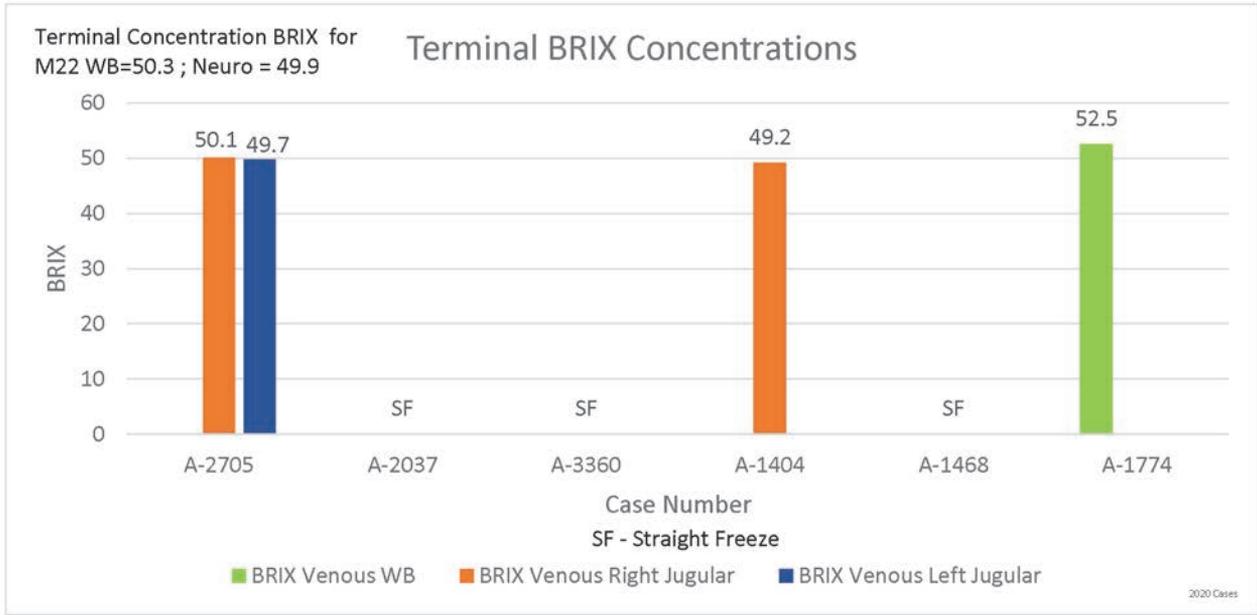
Terminal Cryoprotection Concentration Achieved

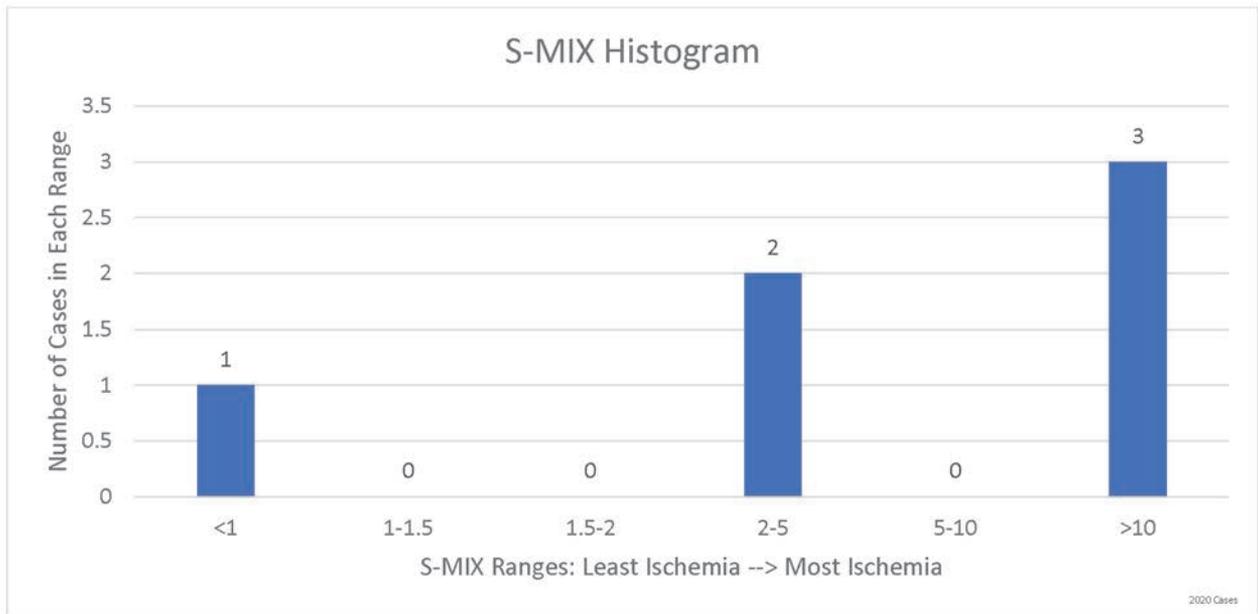


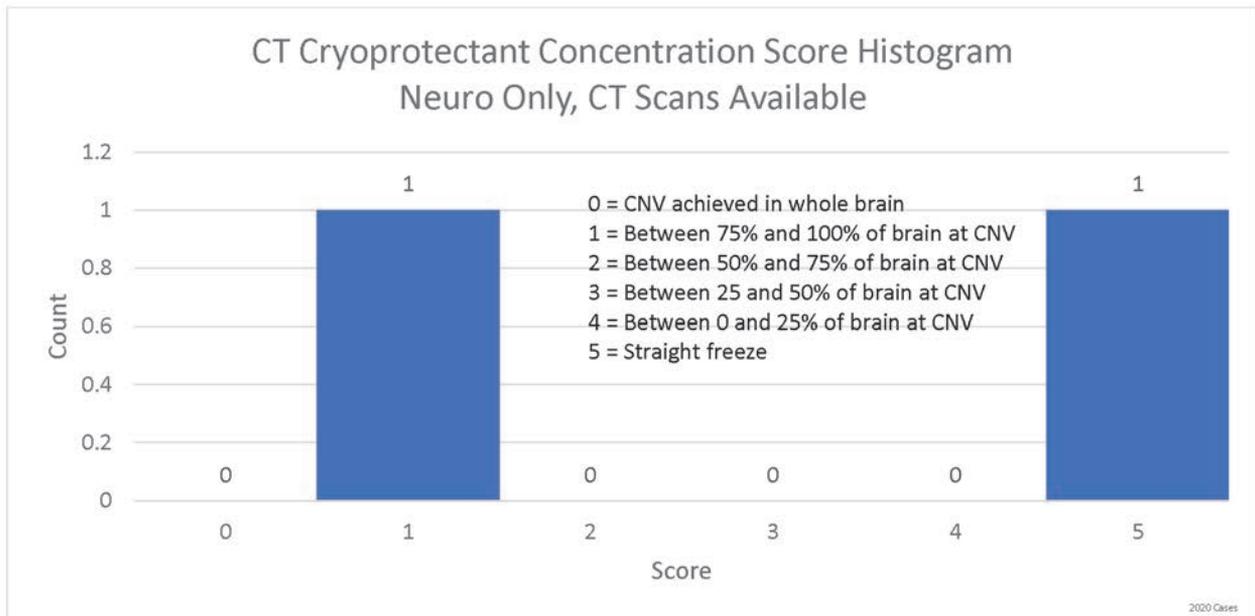
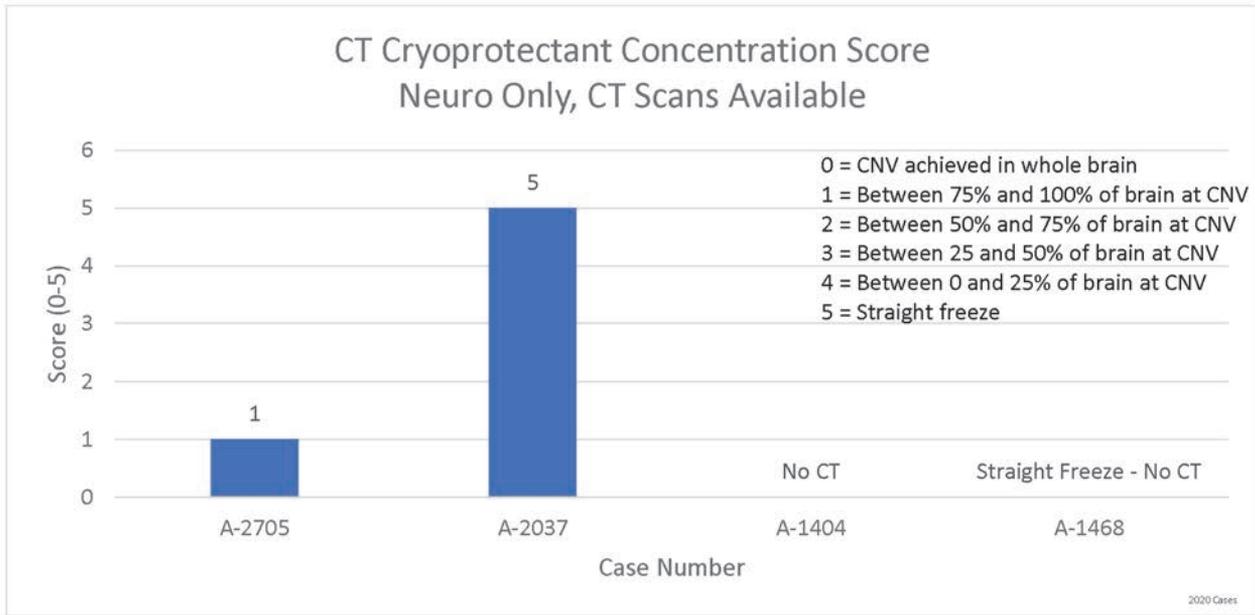
Time from Arrest to First Medication Administration (All Protocols)







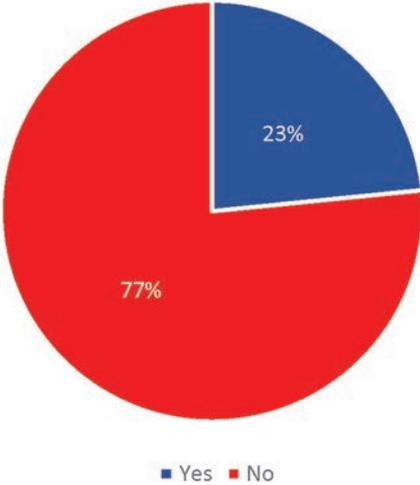




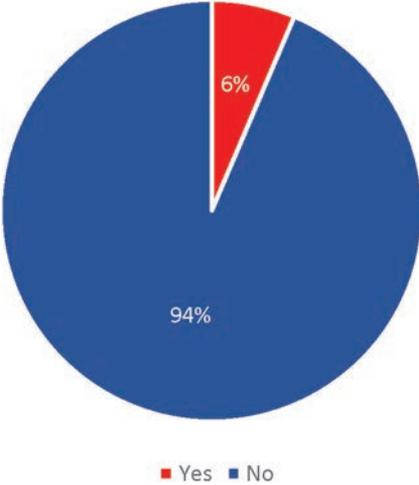
2000 – 2020

141 Cases

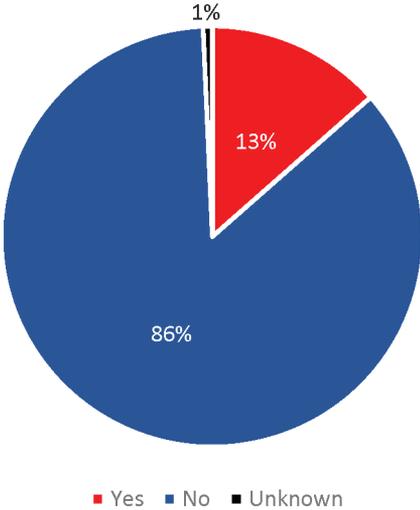
Local Cases



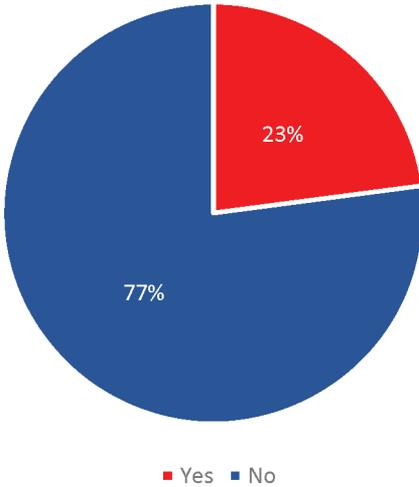
Autopsy



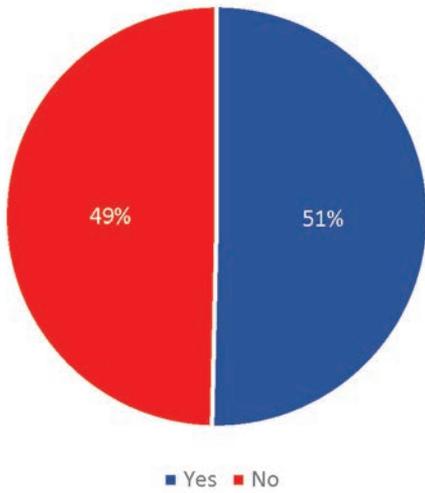
Unattended Deaths



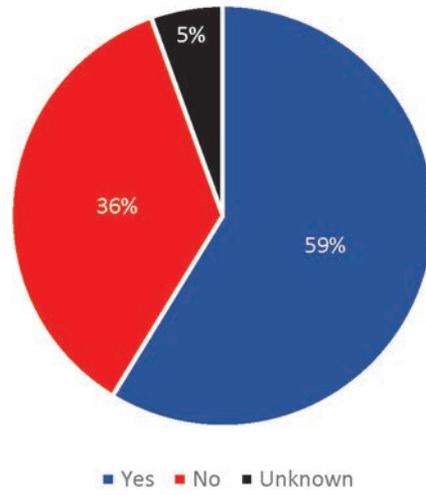
Straight Freeze



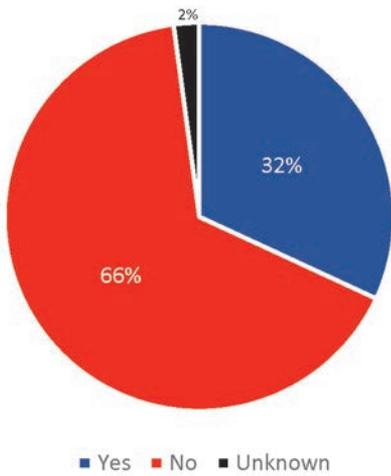
Pre-Mortem Standby



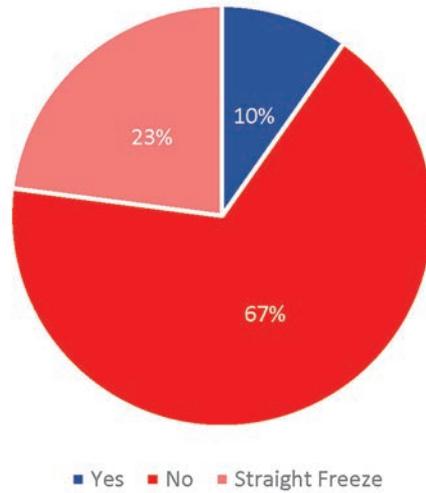
Medications Administered-Full Protocol



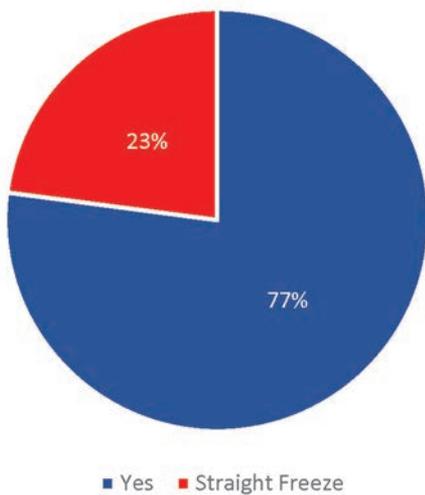
Cardiopulmonary Support
(Chest Compressions & Ventilation)



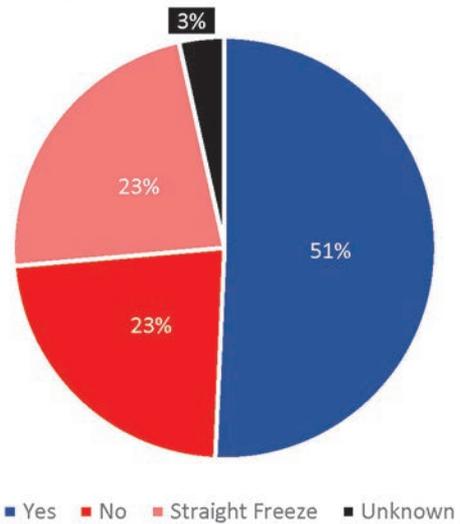
Field Cryopreservation



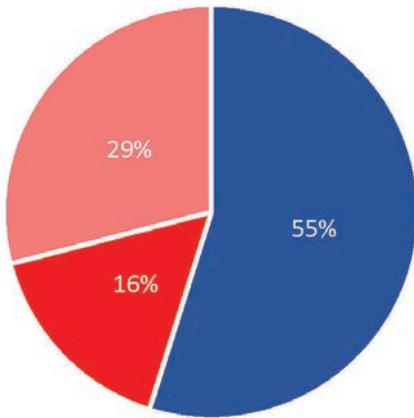
Cryoprotective Perfusion



Terminal Cryoprotection Concentration Achieved

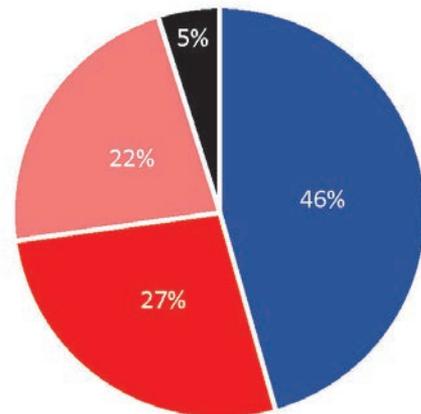


Terminal Cryoprotection Concentration Achieved Whole Body Cases



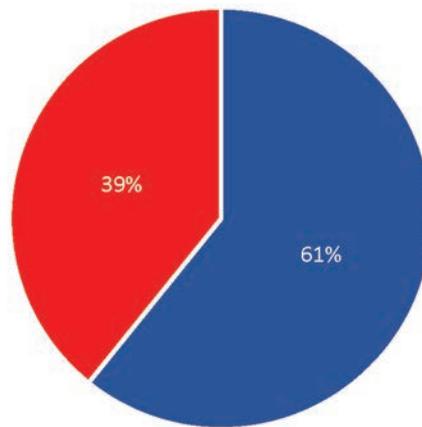
■ Yes ■ No ■ Straight Freeze

Terminal Cryoprotection Concentration Achieved Neuro Cases

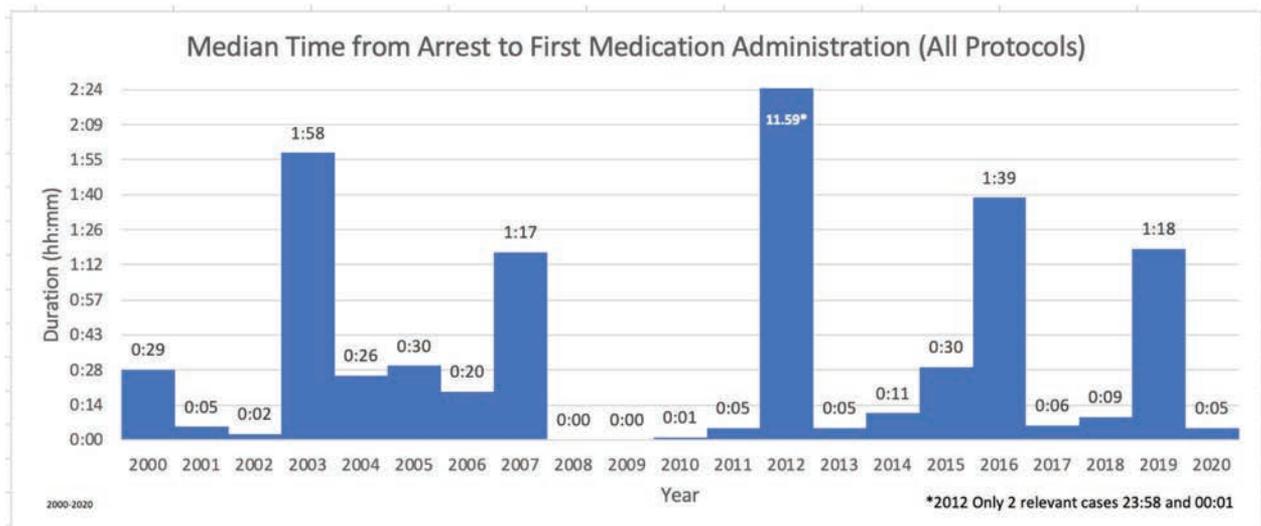


■ Yes ■ No ■ Straight Freeze ■ Unknown

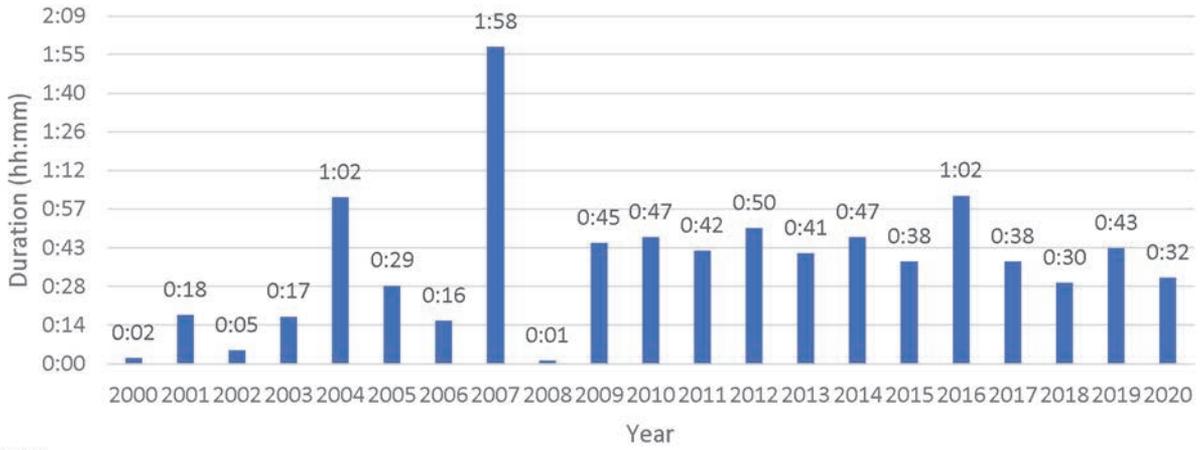
CT Scan Post Cooldown (Neuro Only, Non-Straight Freeze)



■ Yes ■ No

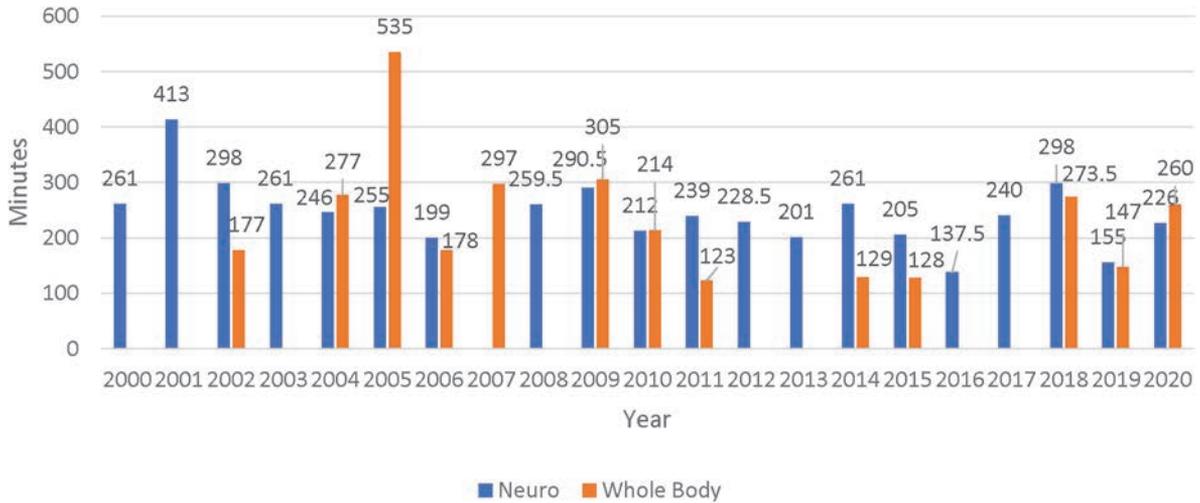


Median Duration of Medication Administration-Full Protocol by Year



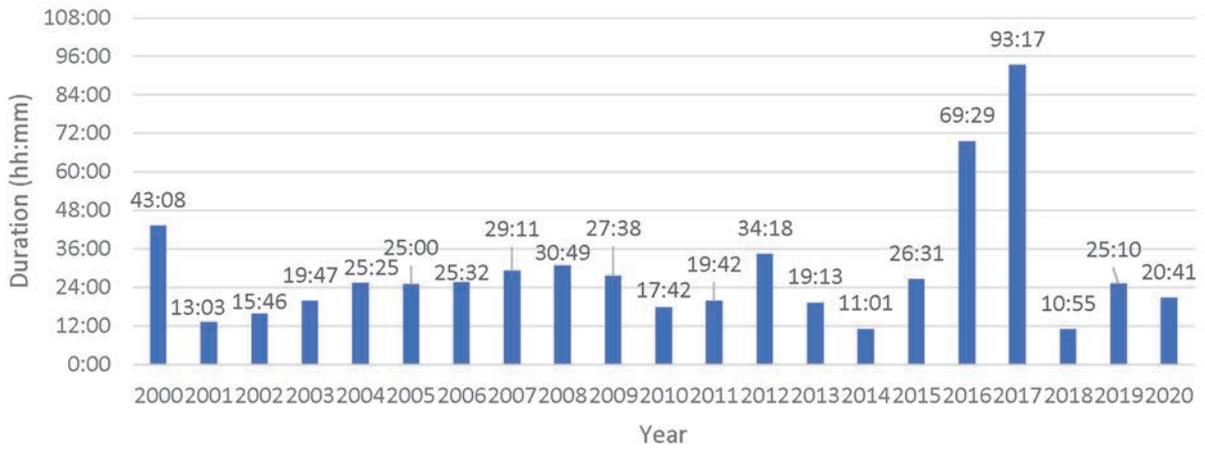
2000-2020

Median Duration of Cryoprotective Perfusion by Year



2000-2020

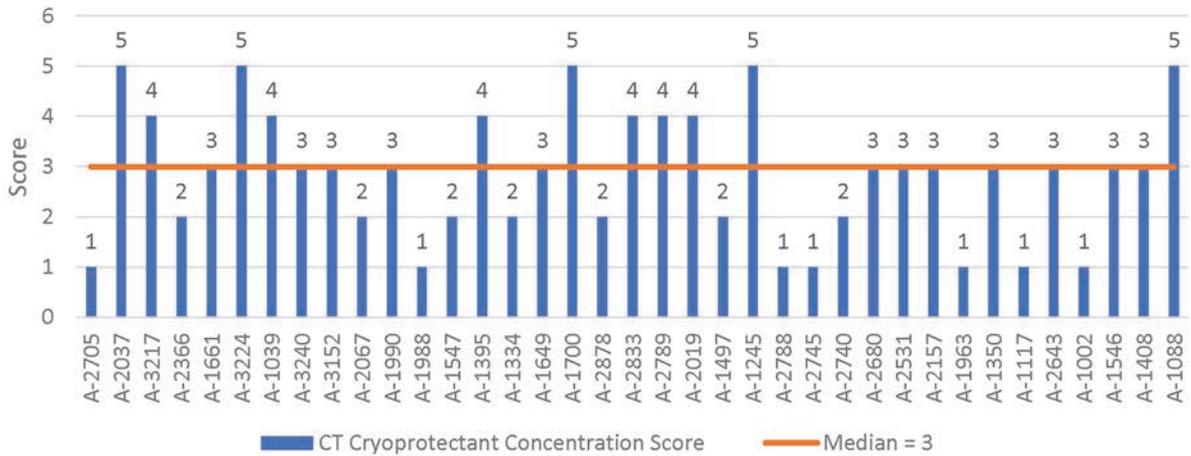
Median Time From Circulatory Arrest to Cryogenic Cooling By Year



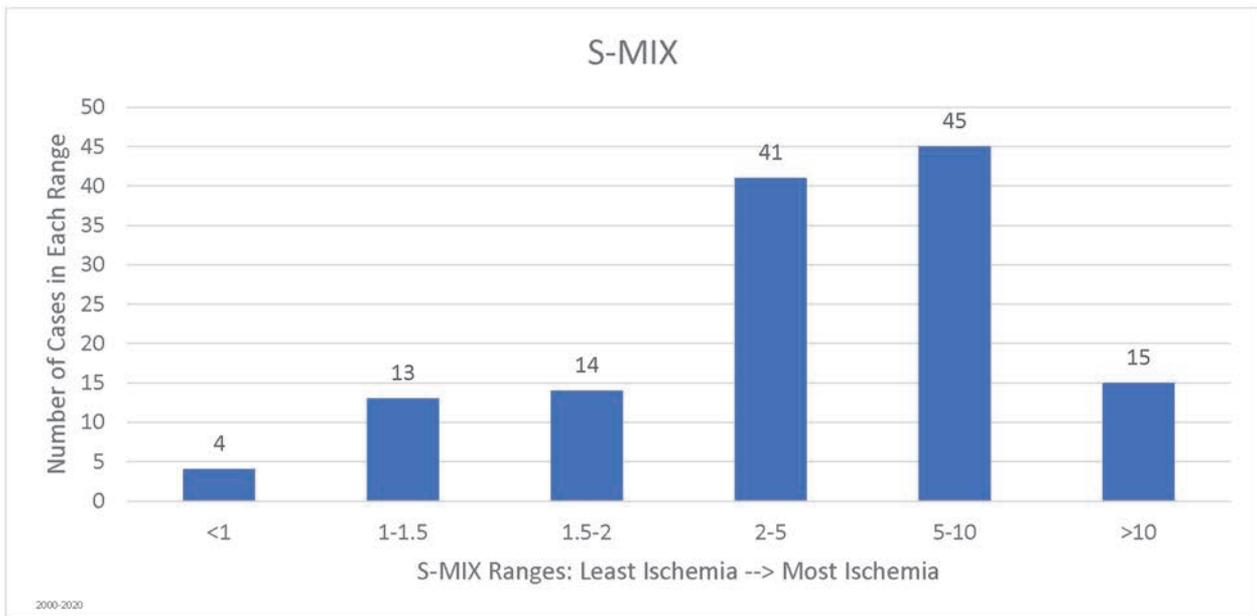
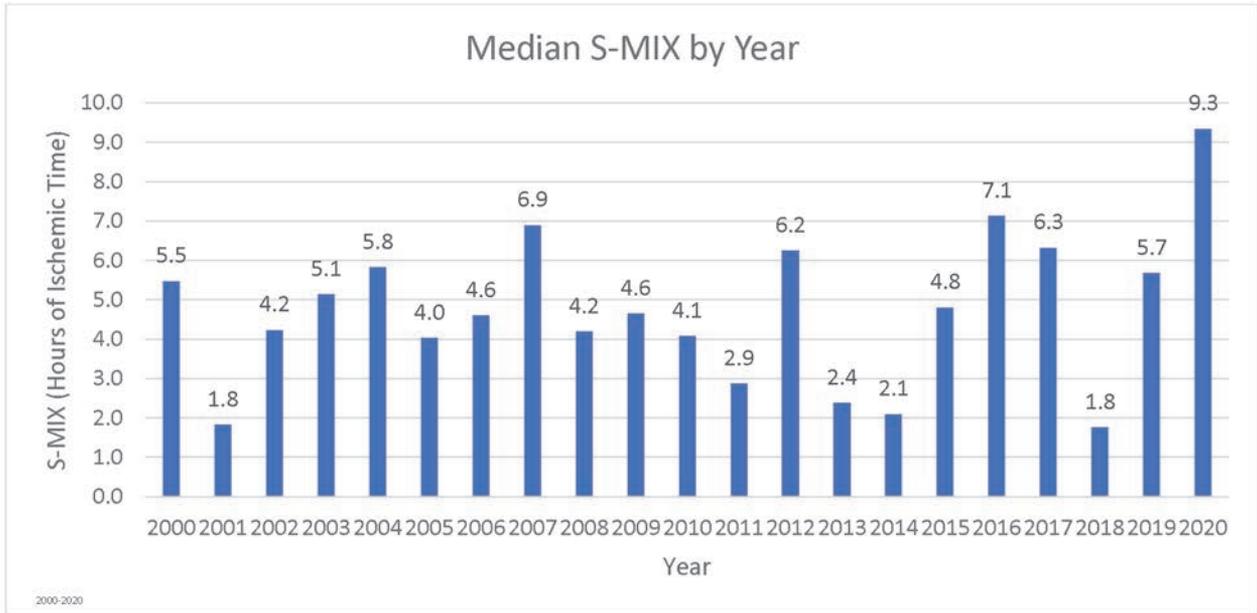
2000-2020

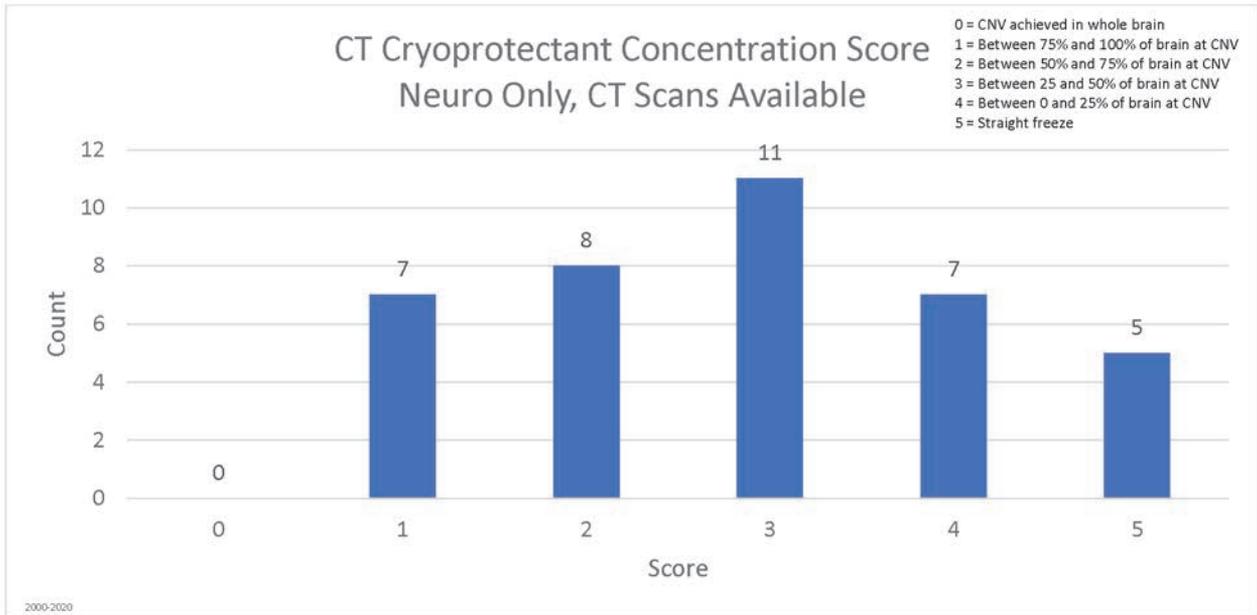
CT Cryoprotectant Concentration Score Neuro Only, CT Scans Available

- 0 = CNV achieved in whole brain
- 1 = Between 75% and 100% of brain at CNV
- 2 = Between 50% and 75% of brain at CNV
- 3 = Between 25 and 50% of brain at CNV
- 4 = Between 0 and 25% of brain at CNV
- 5 = Straight freeze



2000-2020





Alcor Case Metrics: Scope and Comments

By Aschwin de Wolf and Michael Benjamin

The Alcor meta-analysis projects collects and organizes case data for all patients. It is easy to lose track of the bigger picture. To show readers the progress that has been made to date, we present here the first series of case metrics for the years 2000-2020. This cut-off point was chosen because the in year 2000 Alcor started perfusing its patients with a vitrification solution (initially, only neuro).

Selecting a number of case metrics out of many possible metrics raises the question why these metrics and not others. At this point we simply claim that we consider these metrics the most important for evaluating the quality of care at Alcor. Whether to omit, add, or refine some of our metrics is something that we will learn from feedback.

One of the biggest concerns about publication of these metrics is that without knowing the specific context of a case it is difficult to establish whether a “poor” outcome (or trend) is something that was beyond Alcor’s control or not. This topic was discussed in quite some detail at Alcor’s SST Committee meetings. A consensus emerged that while some external events and decisions can sharply reduce Alcor’s ability to provide optimal care given specific policies, ultimately it will be beneficial to treat all bad outcomes as something that is within Alcor’s responsibility to improve. For example, at first sight it seems that an event such as an unattended death of an elderly member who lives alone is not something Alcor can greatly influence. Upon further reflection, this is not the case if we consider that Alcor can allocate resources to providing a daily check-in service for such members, as Alcor has now started doing. If we find that most out-of-state cases show a significant amount of ice formation in CT scans, renewed efforts can be made to provide members with incentives to relocate to Arizona when terminally ill. Another effort could entail providing more field cryoprotections when we consider transport times to the facility too long. In the short run, some events that transpire during a case seem to be beyond Alcor’s control, but in the long run Alcor can design and implement policies to reduce the frequency of those events. One of the reasons for doing the meta-analysis project is that it will more easily identify opportunities for new or enhanced policies to produce substantial improvements.

Fundamentally, the two most important metrics to assess the quality of a cryonics case are ischemia and ice formation. In an ideal case, ischemia is equal to zero and ice formation is equal to zero. Most other technical case metrics can be reviewed in light of these benchmarks. If and when Alcor would consistently deliver on these metrics (which is not yet the case), finer criteria can be added such as viability assays of brain tissue samples after cryoprotection.

The series of metrics that we present here have been divided between presenting the metrics for each case for the years 2019 (the year the meta-analysis started) and 2020. We do not intend to publish such detailed annual metrics prior to the year that the meta-analysis project started but all that data is available to us and used for year-to-year comparisons.

Quantitative presentation of case metrics presents a number of challenges that need resolution. We can only briefly review a few of them here:

Median vs mean

One thing that became quite clear to us during the creation of these case metrics is that in most cases presenting the average can lead to poor information quality due to extreme outliers. To use a specific, real-world, example, the case in which Alcor prevailed in a court order against a family to have a patient exhumed after months of delay and litigation produced an equivalent normothermic ischemia time (S-MIX) so large that calculating the average for that year would have shown an extremely high S-MIX value, even if all other cases had low S-MIX values. Such a number would not tell us much about Alcor’s general effectiveness to mitigate ischemia through standby and stabilization.

Quantification of ice formation in the brain

Since Alcor started CT scanning its neuropatients a wealth of visual information has become available to determine the degree of successful cryoprotection of the brain. The different colors for cryoprotectant concentration and ice formation shown in the CT scan images gives us a reasonably good estimate of how much of the brain has vitrified. Ideally, software can be developed to quantify these results with precision. At this stage we simply rank the concentration of cryoprotectant achieved in the brain on a scale from 0-5, with 0 representing no areas with sub-vitrification concentrations and 5 being a straight freeze. The reason to represent the best outcome by 0 is motivated by the fact that 0 also represents the best outcome in the ischemia S-MIX metric, which allows us to correlate them. It is important to understand here that a CT scan does not allow us to exactly quantify ice formation because the degree of ice formation cannot be simply inferred from knowing the concentration of a vitrification solution in a specific area.

Precision

In many cryonics cases, comprehensive data is not available for every single procedure. Sometimes data is only available in

intervals, and in other cases data was not collected at all. Faced with missing or incomplete data we face a challenge. Either we simply report this as “not available”, or we make our best estimate. The meta-analysis project uses both approaches. For example, if the scribe sheets do not show evidence of ventilation during CPS, we will *not* assume that it happened because it is in Alcor’s protocol. On the other hand, if we do not have detailed temperature data for a patient but know when the person died and when cooling started, we can estimate the typical temperature decrease of a patient based on models and empirical data in the literature and other cryonics cases. In other words, we generally do not assume that something happened without data to corroborate it but when we know something must have happened (the lowering of the temperature of a patient), we use our best calculations. One important question in the meta-analysis project is how much precision we should aim for. As discussed in the article about implementing the S-MIX, the ideal manner to calculate this measure is to use all temperature data available. This does not mean, however, that until the measure is calculated in this manner it cannot yield powerful insights. Since the meta-analysis is such a huge project, we consider it important not to get bogged down in pursuing precision at the cost of progress. What we hope is that over time the precision of our data and models will continue to improve.

Local cases

Only about 25% of all Alcor cases are “local” cases. This means that the overwhelming majority of patients sustain a significant amount of cold ischemia during transport to the facility. In recent years, a growing number of these local cases have been “field cryoprotections” which, in ideal circumstances, eliminates the difference in ischemic exposure time between local and non-local cases.

Unattended deaths

Unattended deaths are almost invariably associated with poorer outcomes due to extensive normothermic ischemia and/or autopsy. For the last two years the number of such cases has increased, relative to its historical average. Preventing unattended deaths has recently been identified as one of the most important priorities for improving case outcomes.

Pre-mortem standby

For the years 2000-2020 only 50% of Alcor members received pre-mortem standby. By definition, unattended (sudden) deaths do not receive pre-mortem standby and there are also many cases in which Alcor, or a contractor, arrives *after* circulatory arrest has occurred. This number shows the limitations of a centralized SST deployment system.

S-MIX

The S-MIX (Standardized Measure of Ischemic Exposure) for a typical patient is around 5 hours of normothermic ischemia. An S-MIX <1 hour of normothermic ischemia has only been achieved in 4 cases during the 2000-2020 period. A case with a <1 hour S-MIX typically entails ultra-rapid stabilization, ventilation during CPS, and continued metabolic support during washout.

Terminal cryoprotection concentration achieved

Complete equilibration of the brain (or whole-body) with cryoprotectant is achieved in 50% of all Alcor cases. It is important to emphasize that this does not mean that in all those cases the brain completely vitrifies. Refractive index measurements concern the brain (or whole-body) at a *global* level and can co-exist with ischemia-induced regional perfusion impairment.

CT Cryoprotectant Concentration Score

As of writing, there are no CT scans of Alcor patients that show unambiguous visual evidence of the concentration necessary for vitrification in *all* areas of the brain, although there are a number of scans that appear close to this goal (typically these are ultra-rapid response local cases and/or field cryoprotections after “dying with dignity”). More than 50% of Alcor (neuro) cases show concentrations below what is deemed necessary for vitrification in more than half of the brain. ■

Implementing the S-MIX

By Aschwin de Wolf

In the 4th quarter issue of *Cryonics* magazine Michael Perry and Aschwin de Wolf wrote the first exposition of a measure to calculate the estimated total time of equivalent normal body temperature ischemic exposure for a cryonics patient. Because it weights time spent at higher body temperature more than time spent at a lower temperature, this measure provides a more precise measure of ischemic exposure than just calculating the total time between circulatory arrest and the start of cryogenic cooling. This measure also allows for a “discount” when metabolic support is provided through ventilation. In an ideal scenario metabolic support would be provided throughout all parts of the procedure, producing an S-MIX value of zero (or close to it). In the metrics provided here the S-MIX is calculated by dividing the total ischemic time in segments, ideally corresponding to distinct procedures (cardiopulmonary support, surgery, blood washout etc.) which allows applying discounts to parts of the case where metabolic support was available. In practice, this approach can only be an approximation because there can be (brief) interruptions of metabolic support and the efficiency of ventilation can vary. To simplify matters we assumed a metabolic discount of 50% when ventilation was performed during CPS.

In the segmental approach we calculate the S-MIX for a given temperature decrease between a start and end time of a procedure (for example, cardiopulmonary support). It should be noted that this approach is a simplification because the cooling rate from the start to the end of a segment is not identical. To remedy this, we calculate a segment under the assumption of Newtonian cooling in which the cooling rate decreases as the difference between the cooling medium and patient temperature decreases. An even more precise calculation would use all the actual measured temperature data available for a case. This is an approach we aim to implement later in the meta-analysis project, which will allow us to compare both approaches. One of the challenges with this approach is that comprehensive temperature data is only available for a few select cases.

How to incorporate metabolic support in the S-MIX is a complicated issue. In our first exposition we allow for a 50% discount in the S-MIX if ventilation is provided during cardiopulmonary support. If this is followed by oxygenation during washout we give a 100% discount. This approach is open to several objections. Giving a 50% discount for ventilation is somewhat of an arbitrary number meant to reflect the lower cerebral perfusion pressure that can be obtained by (mechanical) chest compressions. Whether this number is reasonable is difficult to determine without doing cerebral oxygenation measurements

in the patient, or at least modelling various scenarios in a research model. Another complication arises when a higher metabolic discount is allowed for oxygenation during washout (and cryoprotectant perfusion). One might argue that the dissolved oxygen in washout solutions and cryoprotectants will provide adequate oxygenation of the brain, even in the absence of actual oxygenation. So far we have assumed that oxygenation is always beneficial for the patient without considering the possibility that for some patients oxygenation will actually be detrimental. This topic is mostly unexplored in a typical cryonics context and requires more experimental investigation as well.

The typical cryonics patient may have accumulated (regional) metabolic deficits during the agonal phase as well. This is not taken into account in the way the S-MIX is currently calculated. The most obvious reason for this is because we know so little of the metabolic state of the brain in the typical cryopatient.

In principle, the S-MIX can be calculated for any temperature. At this point, we calculate the S-MIX for all procedures up to the point that cryogenic cooling starts (typically around 0 °C). In principle, the S-MIX can be calculated for sub-zero temperatures but in practice this adds little additional value because the time spent at subzero temperatures before solidification is so short that very little equivalent normothermic exposure time is incurred. The only relevant exception to this concerns storage at dry ice temperature, which can occur as a temporary low-temperature storage measure (for example, when cryonics arrangements still need to be finalized) or after field cryoprotection. The table below shows the S-MIX for storage at dry ice temperature (-78°C), based on $Q_{10}=2$.

EXPOSURE, IN DAYS	S-MIX IN MINUTES
1	0.50
2	0.99
3	1.49
7	3.48
14	6.96
31	15.41
62	30.83
186	92.49

As can be seen, even storing a patient at dry ice temperature for half a year “only” generates an equivalent normothermic ischemic exposure of about 1.5 hours. This estimate is likely to be on the conservative side given that the patient is either frozen or has a highly viscous vitrification solution in his system, which

inhibits most or all diffusion-based biochemistry. One positive consequence of these calculations is that it can support the practice of holding a patient on dry ice for extensive periods when long-term cryogenic storage arrangements are being arranged.

Unlike a straightforward task like calculating the duration of a procedure (for example, cryoprotectant perfusion) the S-MIX is a good-effort *approximation* of the degree of ischemia in a patient's brain. One thing we hope to do in the later stages of the Alcor meta-analysis project is to experimentally model and validate some of the assumptions made in the S-MIX calculations. We will also seek to correlate the S-MIX of a patient with CT scan results to further understand and quantify the relationship between ischemic exposure and the quality of cryoprotection. Like the meta-analysis project itself, the development, validation, and refinement of a quantitative ischemia measure is a work-in-progress that evolves as we learn more. ■

Start preparing your

MEMORY BOX ...now!



Start your own time-capsule!

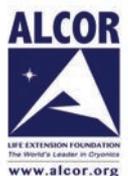
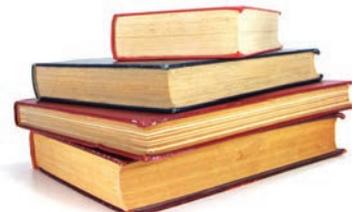
Create a Memory Box with items to augment your memories when you are resuscitated.

No one knows better than you what you will want to have with you.

Alcor makes available to every member and patient, without charge, one acid free Memory Box about the size of a standard banker's box (H10" x W12" x L15") for memorabilia to be stored underground at a commercial storage site called Underground Vaults and Storage (UGVS) in Kansas. Additional Boxes are a one-time charge of \$250 each for perpetual storage.

Some of the most popular items that have been placed into storage are such things as letters, cards, photographs, diaries, journals, notebooks, books, clippings, army records, directories, recipes, video tapes, cassettes, medical records, flash drives, and external drives.

If you would like to begin working on your own Memory Box, or perhaps contribute items to a Box for an Alcor Member already in stasis, or if you have any questions, please contact **Linda Chamberlain** at linda.chamberlain@alcor.org.



A Look Back: Attempts to Establish a Cryonics Community

By R. Michael Perry, Ph.D.

Introduction

Cryonicists are often known to second Saul Kent's opinion, expressed long ago, that being cryopreserved is the second worst thing that can happen to you.¹⁰ The worst, of course, is if you are clinically dead and *not* cryopreserved. I point this out to underscore how we in cryonics are not at all eager to have to undergo this process, we just see it as the best of a bad lot of alternatives we are forced to choose from, whether we like it or not. As we get older, the choice looms ever nearer. And all too often, it turns out that cryopreservation, when it occurs, is of substandard quality because the subject arrested under adverse circumstances and the procedure could not be started in a timely manner. In a typical case, an elderly cryonicist had been living alone, with limited social contact, and was discovered to have arrested in his home only when an expected appointment was not kept or nobody answered the phone when somebody called, and someone started investigating. By then, rigor and massive clotting had set in, and only a straight freeze could be reasonably carried out

Ideas for how to address this difficult problem, not mutually exclusive, include using a system of regular phone calls or other communications with those who might be in need. A more comprehensive approach would use a community of cryonicists who would be in a position to look after each other, especially anyone who is elderly or has a serious illness. A phone service which would be available to Alcor members is currently in the testing phase⁹ and is not the main subject of this report. Instead, we consider the idea of a cryonics community, which has had an interesting, if limited, history.

Two notable attempts were made very early. Evan Cooper acquired a multi-acre plot of land in Maryland, including an old farmhouse, where he hoped to have both a cryonics storage facility and a laboratory. Though strictly speaking only a "business" site not a "residence," his facility seemed on track to become a kind of cryonics community, where people lived as well as (in this case) worked. A parallel effort was begun by Joe Cannon on acreage in Wisconsin. Both Cooper's and Cannon's projects soon ground to a halt, but the idea of a cryonics community persisted, though it still remains, at best, only very marginally realized.

In more recent cryonics history, much of the effort in trying to establish a cryonics community was undertaken by businessman and longtime Alcor member David Pizer. Jordan Sparks also acquired land for his company Oregon Cryonics but decided against having a residence site for cryonicists.

This report starts with some thoughts on a "cryonics habitat" by Mike Darwin. We then consider the Cooper and Cannon projects before going on to David Pizer's efforts, much of which preceded the formation of Oregon Cryonics. Jordan Sparks summarizes his plans for that organization. David Pizer then expresses continuing interest in the community idea and a willingness to "move ahead" with it if needed help from others materializes. Some concluding remarks concern the delicate matter of hastening one's clinical death to obtain a better cryopreservation, and how a cryonics community might further that interest.

Mike Darwin's Thoughts on a "Cryonics Habitat"¹¹

Mike Darwin in a Reddit posting about a place for cryonicists to live or "habitat" is concerned about local amenities and access to medical care. In general, there is a tradeoff: large population centers are best for all services and amenities but the cost of living there is high. For this reason, a more rural living place is preferable, but one must not go too far in that direction, either.

"First, you need to consider access to competent (forget about excellent) medical care. One of these things happened to people who took ill suddenly in the town where I lived; 1) they got lucky and survived 2) they died before they could reach effective medical attention. The EMS [providers] were all volunteer locals and sometimes they could respond and sometimes not. They were also not very good at EMS [emergency medical services]. It took them 20 minutes to get to my house when it was on fire and I lived about 4 miles from the firehouse; get the picture? 3) They received medical attention too late and suffered either unnecessary morbidity or died. This is particularly true in the case of strokes. Elderly people increasingly need routine medical care even long before they are frankly senescent. My partner and I are experiencing this firsthand. You don't just need a doctor; you need the right doctors and you need competent ones. If you get kidney failure you are going to need dialysis 3 times a week. One of my former town's residents had to sell his home at a huge loss because he couldn't make the 1-hour drive each way three times a week."

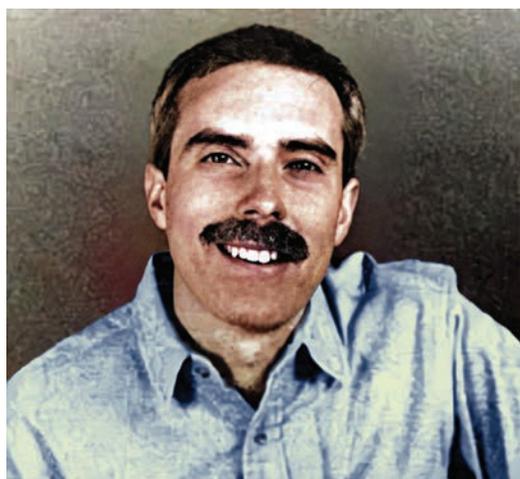
Mike has some further thoughts regarding his living in a small, rural town in southern California:

"A bunch of elderly cryonicists in one spot is worse than useless unless there are facilities nearby staffed by

younger, competent people to treat them. And therein lies the inherent conflict between cost and location. I HATE living where I do now which is in a town with 23K people. The food sucks, there are no worthwhile entertainment venues, and the nearest nice (not mom and pop) restaurant is a 30-minute drive to Palm Springs which, BTW, is a small city of 44K people, but at least has some of the amenities of civilization. I despise the sun and the heat and 4 months of the year the temp is not infrequently 110+ deg F. It's 2 hours from where I am to LA on a very good day and not at rush hour."

Mike once lived in a more populous area (Riverside, California, where Alcor was also headquartered until 1994¹⁴). He found it "an acceptable place to live," but "housing costs are very high" (median home price: \$409,000 as of his article in 2019), which prompted his buying a home "in the middle of nowhere." But this too has its downsides.

"A bunch of old people marooned in a trailer park in the middle of nowhere is a terrible idea. Remember, many people may need temporary nursing home care (e.g., after hip or knee replacement) and those facilities also need to be of decent quality and in proximity. People who are serious about this (and I haven't seen any yet) start by figuring out where they can get a cryonics capability to be in a state where MAD [medical aid in dying] is available, and then start to do their homework using tools like this: <https://www.bestplaces.net/> Talk is cheap."



Mike Darwin about 1986.

The focus here is largely on the "consumer" end – what to look for in the way of settings and/or facilities that already exist and usually would be provided by non-cryonicists for the general public. Not overlooked is to have your cryonics service provider as close by as possible, though not much is said on how to go about this. A different perspective is that of thinking of how

cryonicists might provide their own habitat, which brings us to Cooper, Cannon and Pizer and their efforts to provide cryonicists with a place of their own.

Cooper's and Cannon's Facilities, about 1968-70^{4,6}

Though Robert Ettinger usually gets the credit for having started the cryonics movement with his 1964 book, *The Prospect of Immortality*, his contemporary Evan Cooper was also very important. Cooper's Life Extension Society (LES) was the first organization to promote the cryopreservation idea, which it did through a newsletter and conferences. Cooper also made the first serious attempt to establish a facility where cryonics patients could be stored, on a 19-acre tract in Maryland near the town of Frederick. It had an old farmhouse as living quarters, and a laboratory building with basement that Cooper built at the site for ongoing, relevant research and patient storage. (No patients were actually stored there, nor research done, before the short-lived project ended.) Though he doesn't appear to have stated it, his facility in its rustic location was, in effect, a cryonics community in the making. Cooper offered free accommodation at the farmhouse, in return for volunteer work. Residents were expected to be self-supporting and could pursue employment in the nearby towns. One visitor, Harriet Wellisch, left an engaging description of a visit in September 1969:

"It was early in the morning. Loaded down with sketch pads, pencils, camera, et al, I folded myself into Ev's Volkswagen and off we went. It was a long trip from Hyattsville, Maryland where I was staying, to the farm. To say I was thrilled would be an understatement, even Ev's description of how primitive the area was failed to dim my excitement.

"A rough, narrow dirt road surrounded by lush uncultivated greenery led to a small, padlocked fence thrown across the road. Past this and we were on LES land. Our first stop was to pick up a feline of unknown parentage, who wandered onto the land one day and took possession of the property as only a cat can. Cat (well, what else would you call him?) gave me the once over and decided that I was acceptable—thus with Cat purring contentedly in my lap, we drove to the farmhouse.

"I fell in love with the house at first sight. It is an ancient two-story building (with a wing recently added). Tilted at a crazy angle, it is a ramshackled, weathered, eccentric building with a rustic look that is charming—warped logs, falling timbers and all. Inside there is a stove, sink, refrigerator, some furnishings and dominating the front room, a huge pot-bellied stove. It might not be the most comforting place, but it is so delightful. The best thing of all—at least to a city gal like me—is the outhouse. The only thing missing is a crescent in the door. The house is surrounded by a tangled mass of trees and undergrowth

with a liberal sprinkling of aromatic mint, which grows with a persistent abundance, giving the air a refreshing minty breath.

“I took a few photographs, made a few sketches and continued on to the lab, located about a hundred yards from the house. With Cat leading the way, we took a circuitous route, so that Ev could show me the pond. He explained that when properly dammed, it was filled with clean water. Now it was polluted with an edge of white mold (actually slime, but mold sounds so much nicer). Nevertheless, with the gnarled trees growing right down to the water’s edge, it was a romantic picture.

“We walked around a no-path path. The forest was alive with the movement of creatures—some like the leopard frog, I was quick enough to spot before they went into the undergrowth—and yes Virginia, there is a pileated woodpecker!

“The lab is a deceptively simple building which stands out in a clearing overlooking the pond. One thing is apparent, both here and at the farmhouse, a tremendous amount of work has been done. Unhappily, because there are not enough volunteers the work is progressing slowly.”

In the end, Cooper could not obtain the help he needed. The facility, so appealing in concept, with its rustic setting and ability to provide both living quarters and a work and storage environment, had to be abandoned. Cooper himself left the movement by mid-1970 and was lost at sea in 1982.



Laboratory building and pond on Ev Cooper’s land, early spring, 1969.

While Cooper’s drama played itself out, there was a parallel effort at nearly the same time with solid initial success but, in the end, little to show for it, even in the way of an interesting story by an inquisitive visitor. Joe Cannon had financing and was able to construct a facility comparable to Cooper’s laboratory (and actually a bit larger) on a tract of 30 acres near Appleton, Wisconsin. Called Hope Knoll, the project had to be abandoned

before it could get started due to regulatory hurdles (where the facility would have to be treated as a cemetery), when initially it seemed that this problem would not be serious. Though he couldn’t operate his own facility after having built it, Joe remained active in cryonics for many years and, with his wife, Terri, is now a patient at Alcor.



Joe Cannon’s impressive Hope Knoll facility could never get regulatory approval in its home state of Wisconsin.

“Ventureville,” 1995^{15,14}

Many years went by. In February 1994 Alcor, which had been started in 1972, moved its headquarters from Riverside, California to Scottsdale, Arizona. Close by the new site was David Pizer, an Alcor member and cryonics activist who had been instrumental in securing the site. A few years before, in 1986, David had started the nonprofit, cryonics-promoting Society for Venturism. One of the longstanding goals of this effort was to create a cryonics community which would particularly provide inexpensive living space for low-income cryonicists as they aged and approached their cryopreservation. Toward this end, a house was purchased on East Utopia Road in Phoenix in January 1995, renovated with volunteer help, and opened to the cryonics public with the informal name of “Ventureville.” It was not an “all-in-one” community like Cooper or Cannon might have started, just a residence for cryonicists, but well-positioned for when cryonics services would be needed. In an article in the newsletter *Venturist Monthly News* I wrote enthusiastically:

“One of the major problems, having a convenient place to deanimate near a cryonics facility (one is 10 miles away) can now be much better addressed. Cryonicists will now have a place to move to, to be with their own kind and look after each other’s needs. The establishment is to be ‘interdenominational’ and rented to tenants of all cryonics organizations. At present Alcor is the only organization with a nearby facility but others might be expected to follow if the idea succeeds. ...

“The main credit for the founding of Ventureville must go to businessman and principal architect of the Venturist organization David Pizer. This I know has been a dream of his for many years, and with iron



The "Ventureville" house on East Utopia Road, Phoenix, AZ, March 1995;
David Pizer (center) and Scott Herman volunteer with painting.

determination and his personal financial contributions, he has finally succeeded. Scott Herman, a cryonicist who has worked beyond the ordinary obligations of employment, is also to be commended for helping with the renovation, which requires many sorts of expertise as well as sheer sustained effort.

"As I write, the work goes on. Much remains to be done to ready the main building for occupancy, but it is getting done fast. After this there will be the usual efforts to maintain and improve the premises and the Venturist establishment overall, and if time and finances permit, our plans are ambitious. ..."

In all, a few cryonicists rented rooms at the Ventureville site for a year or so. David wanted to get investors to further develop the project (see below) but could not, and, when the renters all left, it was sold.

Creekside Preserve, 2002^{7,16}

The next "Ventureville" project came about when David Pizer purchased undeveloped land near Mayer, Arizona and built a rental facility. Creekside Preserve Resort, which borders on a small body of water named Big Bug Creek, was open to the general public in October 1992. It included about a dozen cabins, several with jacuzzis, and several rooms for occupancy in the main lodge, and was about a 75-minute drive from Alcor.



David Pizer waves from Creekside Preserve lodge on Opening Day, Oct. 27, 2002.

John Grigg wrote an article for *Cryonics* about the Opening Day and the future plans which I've excerpted from here.

"The grand opening of Creekside Preserve resort was held on Sunday, October 27, 2002, at the Creekside Lodge in Mayer, Arizona. The Creekside resort is presently open to the general public including cryonicists (of course!), but it is the hope of many that a special cryonics community ("Ventureville") can be completed here in reasonable time"

The event including dinner was hosted by David, his wife Trudy, and John himself. John found it a "fun and intimate gathering" with many interesting activities and meetings with friends and acquaintances. Before getting started, John and others were standing on an elevated porch on the back side of the lodge, with a view of the creek and the hills beyond it, and a deer approached.

"We watched ... as this beautiful creature carefully hopped from bush to rock until it was at the creek for a Creekside Preserve/Ventureville drink. Then it carefully worked its way back over the hill and was gone. Mr. Pizer pointed out that often guests will be able to see a herd of deer or javelina (wild native pigs), or other animals and birds come to the creek for water."

John and David then gave a tour of Creekside starting with the main lodge.

"Our visitors had already seen the great room with its beautiful western furniture, large fireplace, and western artwork, so we started at the basement level to view the gymnasium and the conference room. The conference room holds 100 to 120 people, and the possibility of using it for Alcor meetings instantly flashed in the minds of some of those present.

"Next, with Albert, Mr. Pizer's great, ebony-coated great dane padding powerfully in the lead, we headed out to the cabins. Their upscale quality impressed everyone, and as usual the bright red, heart shaped, hot tub/jacuzzis got everyone's approval! Creature comforts such as a microwave oven, cable TV, mini-fridge, gas fireplace, and even a dimmer light make

each cabin very inviting. Some of them have a king-sized bed; others have two double beds and no jacuzzi. We also have two cabins that can accommodate handicapped guests. We stood out on one of the cabin porches that overlooks the beautiful creek site as Mr. Pizer explained about the area. The natural beauty has been preserved, and it is a wonderful experience to spend time on those large, covered porches.”



Cabins at Creekside. Hikers, from left: Hugh Hixon, Bill Haworth, David Pizer, Joe Hovey, John Grigg (author was also with the group, taking picture). Observatory is visible as small detail on hilltop, upper right.



Hikers face the (author’s) camera: from left: David Pizer, John Grigg, Hugh Hixon, Bill Haworth, Joe Hovey, author as inset (from photos by John Grigg).

After this, “we hiked further around the property,” first to horse stables, then to an observatory David had built on the highest hill of the 34-acre site. The guests “oohed and ahed at the powerful, 12-inch Schmidt-Cassegrain telescope, and Jerry Searcy [a longtime stargazing buff and now a patient at Alcor] quickly volunteered to be our resident visiting astronomer!”



Observatory. John Grigg (left) and Hugh Hixon inspect.

“We were on the high ground looking down at the lodge. It was then that Mr. Pizer shared with us his vision for a complete community where a cryonicist can come to live among others with similar interests and beliefs. First, he noted that, when possible, he will build 30 or so more cabins to increase the profits of the resort part of the community and provide a financial base for the cryonics interests. Next, he pointed to a low, flat hill and said a recreation center would be built there, a large building with a gym, meeting rooms, a club house, and a swimming pool that was half inside the building and half outside. It will be open for both the Creekside guests and the Ventureville residents. It will have places for cryonicists to relax, play, work, and study. Someday, the Venturists would like to build a library and a cryonics museum in the area.

“Mr. Pizer then pointed in another direction. About 20 apartment units and some private houses would be erected there. He emphasized his desire to make these affordable to those who would want to come here, but also to have large homes for those who could afford them. ... It will be a community where we will work together to advance the cause of cryonics, and an end to death, based on whatever talents we have to offer.

“... It was a beautiful morning. It had been raining the night before; now the sun was peeking out. The raindrops glistened on the leaves of the trees and bushes, giving them a twinkling, magical appearance. Some of the moss on the granite boulders was wet and seemed fluorescent. The whole desert was clean and bright and with the feast to the eye and drink of the conversation it was a high point for all in attendance. ...”

One of the attendees was Dr. Jerry Lemler, then CEO of Alcor, who gave an after-dinner talk.

“He started out by thanking David Pizer for his hospitality and the beautiful place he had built. Then he told us of the new plan to have standby service available to all Alcor members at no extra cost to them if they sign up by June 2003! The old days of having to have a big bank account to cover the cost of extended-length standby teams are soon to be over. There were caveats in his presentation that would depend on how the Alcor Board felt.

“Next, Dr. Lemler shared how only the night before he had come to a firm decision to have the Alcor equivalent of a ‘Ronald McDonald’ house. This will eventually mean a dying person can come to an Alcor hospice and bring the whole family along! Mr. Pizer pointed out this will really increase the number of people who, by getting the support they and their family need, will actually get suspended.

“Dr. Lemler in his talk asked Mr. Pizer if he would help in finding Alcor a suitable property for this endeavor, and in any other way he could. Mr. Pizer responded that he would either help Alcor find a property in the Scottsdale/Phoenix area or would entertain discussions for having that facility in, or near, Creekside/Ventureville, if that is what the Alcor Board wanted. It was brought out by Mr. Pizer and Dr. Lemler that when a person becomes terminal, they do not want to leave their home and go to a strange place to die. If there was a retirement center and hospice in or near Creekside/Ventureville, people could come and visit while healthy and when the dying time came, they would be going to a place they were familiar with and would therefore probably be more comfortable. It was also emphasized that a person is likely to get a better suspension if he/she deanimates near Alcor.



Alcor CEO Dr. Jerry Lemler at the gathering where he spoke.

“It was an excellent and very heartfelt speech. At its conclusion Dr. Lemler was met by energetic applause. I knew at that point this was no ordinary little cryonics gathering! Overall, it was a wonderful experience for me. I got to know many of the Alcor staff much better. And networking among us and our guests will, I’m sure, bear much fruit down the road. It was sad to see everyone leave, but at least Dr. Perry and I had taken a lot

of pictures to remember the day! My personal thanks to everyone who came, and I hope those of you who

couldn’t make it for whatever reason this time will be able to attend our next one!”

After this there were other, similar gatherings at the Creekside Resort as the years went by, the last important one being in 2012. The operation was certainly better managed and better financed than Cooper’s had ever been, and there was no regulatory problem like what had stymied Cannon, but in the end the property was sold. No cryonics community as envisioned materialized. The property still functions as a resort, open to the general public, but the new owners have not shown interest in cryonics.

Oregon Cryonics Demurs on “Community”⁷

Located in Salem, Oregon, Oregon Cryonics (OC) “was established in 2005 as a Non Profit Mutual Benefit corporation. It is not charitable, public benefit, or tax exempt. It actually operates very similarly to a for-profit corporation, except that the assets are protected from being taken by the director(s).” Carrie Wong in a 2015 *Cryonics* article offers some further background on the organization, and its founder and executive director, Jordan Sparks, D.M.D.:

“... Oregon Cryonics is licensed as a Non-transplant Anatomical Research Recovery Organization (NARRO) which is authorized by the State of Oregon to accept bodies donated under the Uniform Anatomical Gift Act (UAGA). Jordan Sparks signed up for cryonics over 20 years ago while he was still in dentistry school. He has been an active member of the cryonics community and was on the board of CI as a director for six years. Jordan’s motivation eventually went even further than being a director of CI and he started collecting and fabricating his own cryonics equipment for a number of years before he started Oregon Cryonics. Although he had been a practicing dentist for a decade, he got his big financial break in the software company he created: Open Dental. Open Dental has doubled in size since 2003 and in 2014 it brought in an annual revenue of over \$5 million with over 50 employees. His dental software company’s success has allowed him to fully dedicate his time and resources to Oregon Cryonics.”

With commendable dedication and self-funding to match, Jordan is pursuing his ideas of the best possible cryonics facility, on property he has acquired. A recent posting at OC’s website confirms, however, that he does not feel his organization’s property and resources should be used to house a community of cryonicists:

“Over the years, I’ve purchased some land to expand my software company. In the process, I’ve ended up with seven rental houses, so I’ve naturally toyed with the idea of building a cryonics community. At one point, I even had plans drawn up for an RV park on part of the

property. But here's the problem: Renting houses or RV pads must be done as part of a well-run business, and that requirement does not match up well at all with the goal of building a cryonics community. A given cryonicist applicant would need a down payment, be able to pass a credit check, commit to a lease, and even potentially be evicted for failure to pay rent. If I want to make exceptions for cryonicists, how would I decide who to make exceptions for, and how far would the normal policies be stretched? Is claiming to be a cryonicist good enough to get a free house? For how long? This sort of thing can easily end badly. It's also very unlikely that the timing could work out. Should a certain number of spots be kept open in case a cryonicist comes along? That seems expensive. Let's also not forget that some of these cryonicists may be near death. So now, we're really talking about also needing a nursing home. Running a nursing home is far beyond my capability unless I dedicate 100% of my energy to that job alone. ..."

David Pizer Remains Positive³

Jordan Sparks, it should be noted, is not being negative about a cryonics community in general, just does not want it as part of his facility. David Pizer does not operate a cryonics facility and remains positive on his views of the community idea. He was recently contacted and agreed to the composite interview with the author and Aschwin de Wolf that follows.

What are your thoughts on the advantages of having a cryonics community?

I believe the time is now ripe for a cryonics community to be created in the United States.

The amount of people signed up for cryonic suspension that are living in the USA is now a large enough population that there should be a strong customer base for a facility to offer living quarters and other benefits to cryonicists.

Would you elaborate on how such a community would operate, would cryonicists pay rent, etc.?

I would recommend the people who want to make available and manage this facility create a for-profit corporation to own and manage the company. The articles of incorporation could provide safeguards to see that the company is suitably run and for-profit ownership would provide the incentive to make sure that the income of the company was to be continuously more than the expenses, the goal [being] that once established, the community would be able to remain in business and be able to grow as the demand for their services grows at the same rate as cryonic suspension providers is growing.

How would such a community be managed?

Here is how the initial effort to get started might work:

A group of individuals and entities (established cryonics support organizations and/or suspension providing organizations), could join together and work out the rules and goals of the organization.

The founding group would be individuals who would each agree to purchase a specific amount of stock when the corporation is formed and would deposit 10% of their purchase pledge in a bank account while the attorneys are helping us create the Articles of Incorporation and the Bylaws.

Nonprofit organizations could also be stockholders in this entity. And they would also put up 10% of the total amount they intend to buy in at when the paperwork is completed, and the corporation is ready to sell stock.

As the work on creating the corporation's Articles of Incorporation and Bylaws moved along, voting on how to proceed at each step would be done by each person or entity involved and each would have a percent of the total votes based on their percent of the total amount of money that had been deposited in the starting bank account.

For example, if a person had put up \$100 (as a deposit on eventually purchasing \$1,000 worth of stock when the corporation was ready to sell stock), and there was \$10,000 total in the account when the vote on something came up, that person would have put up 1% of the total money so far, and so that person would be allowed to have 1% of the total votes.

Another person who had deposited \$500 into an account with a current balance of \$10,000 would have 5% of the total votes.

Of course, once the corporation was up and running its Articles and/or Bylaws would provide a way of voting based on how many shares of stock each investor owned.

Management would grow older, retire, hopefully get cryopreserved themselves, and new management would have to replace them. How would you provide for this?

The beauty of a for-profit corporation provides for how officers and employees are replaced when need be.

Would your community cater to non-cryonicists as well as cryonicists?

If you want a true cryonics community, I would suggest only renting to signed up cryonicists.

Nowadays, renters have certain rights against the owners and managers of the buildings they are renting space in. Having non-cryonicists as tenants along with cryonicists as tenants opens the door for a way a non-cryonicist could easily harm the corporation if they ever got angry about most anything they didn't like that might come up.

How would you deal with aging and ailing cryonicists, particularly those who would feel their “time has come” and would want to hasten their legal death for better cryopreservation?

Our organization would not want to be involved in hastening legal death matters. Things like that and other important things having to do with cryonics would be pretty much known as residents communicated with each other. Also there could be weekly meetings and events managed by the residents to share information.

Could your community offer hospice services to help those wanting to be cryopreserved?

Many states allow for in-home hospice services. We would not want the added responsibility and liability of our company being a hospice, but residents could use the in-home hospice companies while living at our facility when the time comes.

That means the resident can turn their apartment into a hospice room by employing the services of an unrelated company to provide the needed hospice personnel and equipment. This provides the service the resident needs without us having the expense and liabilities of running a hospice.

Regarding the past Ventureville attempts, how did they get started and what were the challenges?

There never was a formal attempt to build Ventureville. On several occasions I put forward the idea to the cryonics community and I received replies that some people thought it was a good idea and they would be glad to stay there when it was built. But when I talked about donating money to get it going no one volunteered to contribute. My original thoughts were for the Venturists to build it so people could donate and get a tax writeoff. What I learned from that was if there is ever going to be a cryonics community it will have a better chance of raising the money if people can invest in a corporation to buy the land and buildings and own stocks in that corporation, and then that corporation can rent the buildings to a non-profit organization to run the community or the corporation can run the community. Either way the original investors could earn a return on the money they invested and own stock which gives the investors the right to vote on management decisions. So, the challenge was and still is how to raise the money.

Why was the Ventureville effort abandoned?

Since a formal effort (putting a deposit on a site and soliciting money to buy the site) was never started, it was never abandoned. I still would like to be involved in a project like this if a group of cryonicists gets formed and wants to move forward.

What can you say about your efforts to establish a cryonics community more or less by yourself?

For many years I have been interested in creating a cryonics

community through the nonprofit Society for Venturism organization. I finally realized that using a nonprofit to create a cryonics community was the hard way to proceed. There were many people who said they would like to live in a community of cryonicists as there is protection in numbers. But no one of means was willing to donate money needed to build one.

But doing this with a for-profit corporation allows investors a chance to make a profit off their investment while creating a place to live that would increase their odds of getting a better cryopreservation by having neighbors who know what to do if they suddenly died without warning. It is based on the model I used when I created the present facility for Alcor in Scottsdale.

Are you now retired? Do you have any advice for someone else who wants to start a cryonics community?

I am not in retirement; I have bought commercial buildings and rented them out in the past and now I am doing that with houses and I work out of my house. I now have a property manager company to manage my rental property so I can go do anything else that I want to.

I am perfectly willing and able to help in investing in and helping build and manage a cryonics community if there are others who want to join together and start one. I have managed four different resorts in the past and that work is good knowledge for building a cryonics community which has similarities for profit and liabilities of a resort.

Also, I have the experience of moving Alcor to Arizona when California was getting ready to condemn the building they were in and close them down. I found the property in Scottsdale and negotiated a fantastic price for Alcor. I created the Cryonics Property LLC to raise the money from investors to buy the building and rent it to Alcor. I created the opportunity for Alcor to eventually buy the investors out. I managed the business affairs of Alcor for 9 years as their treasurer and Vice President under four different presidents.

Thank you very much for your input.

You are welcome.

Cryopreservation and Hospice Care: Some Closing Remarks^{1,5,13,17}

One concern of aging or otherwise terminally ill cryonicists is to get a good cryopreservation when the right time comes. Nature can be uncooperative, burdening the prospective patient with dementia, for example, even if others are attentive when arrest occurs. Many cryonicists would like to be able to choose their cryopreservation when the time seems right, rather than let nature take its course. Some states now have “death with dignity” provisions for certain cases of this sort. Generally, there must be a terminal illness, such as advanced cancer, with no more than six

months of time remaining, as estimated by medical professionals. Otherwise, one may have a slow, encroaching condition that will lead to mental impairment before “death with dignity” can occur. Such individuals may feel forced to hasten their own legal death, the safest means being voluntary stopping of eating and drinking (VSED) or self-starvation/dehydration. (Choosing this should not incur the threat of autopsy, since legally it is treated as “death by natural causes” not suicide.)

The thought of doing this is not pleasant (though it is said to be not particularly painful) but it could be the best alternative under the circumstances. A variation known as palliative sedation, sometimes though not always available, maintains a metabolic coma or near-coma until arrest occurs. Though palliative sedation often is prescribed to alleviate intractable pain or suffering in recognizably terminal cases, there is also a category known as “existential suffering” in which death is not imminent nor is physical pain acute when the treatment is started. Instead, there are other compelling reasons to proceed. For a cryonicist this might include early recognized stages of a dementia-threatening but slowly progressing disorder. Examples include Alzheimer’s disease, vascular dementia, and other aging-related conditions.

The question comes up of whether living in a community of sympathetic cryonicists would further the interest of hastening one’s cryopreservation under circumstances where this course seems the preferred one. David has indicated that the community should not be in the business of providing services itself toward this end. But it might be handled through the home hospice option, in which the arrangements are made by the individual, apart from the property management. These matters call for further discussion. ■

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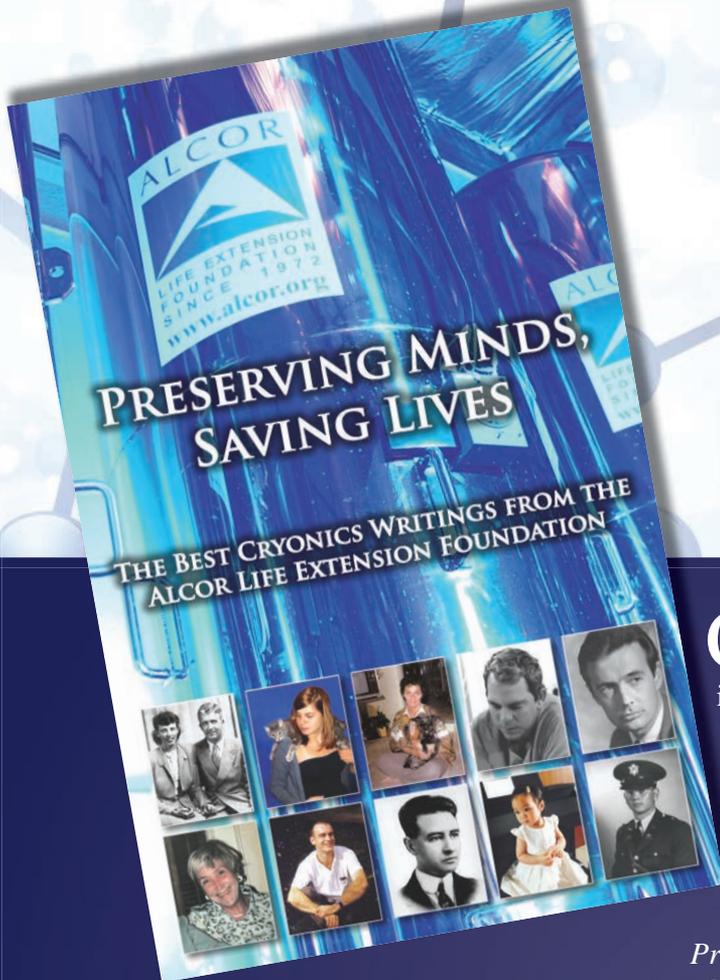
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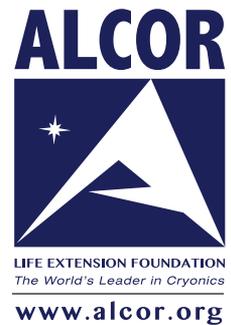
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Fight Aging!

Reports From the Front Line in the Fight Against Aging

Reported by Reason

Fight Aging! exists to help ensure that initiatives with a good shot at greatly extending healthy human longevity become well known, supported, and accepted throughout the world. To this end, Fight Aging! publishes material intended to publicize, educate, and raise awareness of progress in longevity science, as well as the potential offered by future research. These are activities that form a vital step on the road towards far healthier, far longer lives for all.

Supporting Evidence for the Hypothesis that NAD⁺ Upregulation Increases Cancer Risk

January, 2021

NAD⁺ levels in the mitochondria decline with age, and this is a proximate cause of reduced mitochondrial function. Approaches to increasing levels of NAD⁺ in aging cells have been shown to improve metabolism and mitochondrial function in mice, but the evidence is mixed in humans for there to be any meaningful effect on age-related conditions. The common approaches to NAD⁺ upregulation, meaning supplementation with derivatives of vitamin B3, such as nicotinamide riboside, are about as effective as structured exercise programs in increasing NAD⁺ levels.

There is the suspicion that taking this shortcut - without adding all of the other metabolic effects of exercise - could increase the harms done by problem cells in the aging body, such as senescent cells and cancerous cells, by allowing them greater activity. The evidence is sparse for this to be the case, but it is a concern amongst researchers. The research noted here adds a little more weight to the concern side of the scales.

In the 1920s, German chemist Otto Warburg discovered that cancer cells don't metabolize sugar the same way that healthy cells usually do. Since then, scientists have tried to figure out why cancer cells use this alternative pathway, which is much less efficient. Researchers have now found a possible answer to this longstanding question. They showed that this metabolic pathway, known as fermentation, helps cells to regenerate large quantities of a molecule called NAD⁺, which they need to synthesize DNA and other important molecules. Their findings also account for why other types of rapidly proliferating cells, such as immune cells, switch over to fermentation.

Fermentation is one way that cells can convert the energy found in sugar to ATP, a chemical that cells use to store energy for all

of their needs. However, mammalian cells usually break down sugar using a process called aerobic respiration, which yields much more ATP. Cells typically switch over to fermentation only when they don't have enough oxygen available to perform aerobic respiration. Warburg originally proposed that cancer cells' mitochondria, where aerobic respiration occurs, might be damaged, but this turned out not to be the case. Other explanations have focused on the possible benefits of producing ATP in a different way, but none of these theories have gained widespread support.

Researchers treated cancer cells with a drug that forces them to divert a molecule called pyruvate from the fermentation pathway into the aerobic respiration pathway. They saw that blocking fermentation slows down cancer cells' growth. Then, they tried to figure out how to restore the cells' ability to proliferate, while still blocking fermentation. One approach was to stimulate the cells to produce NAD⁺, a molecule that helps cells to dispose of the extra electrons that are stripped out when cells make molecules such as DNA and proteins. When the researchers treated the cells with a drug that stimulates NAD⁺ production, they found that the cells started rapidly proliferating again, even though they still couldn't perform fermentation.

This led the researchers to theorize that when cells are growing rapidly, they need NAD⁺ more than they need ATP. During aerobic respiration, cells produce a great deal of ATP and some NAD⁺. If cells accumulate more ATP than they can use, respiration slows and production of NAD⁺ also slows. Therefore, switching to a less efficient method of producing ATP, which allows the cells to generate more NAD⁺, actually helps them to grow faster. "Not all proliferating cells have to do this. It's really only cells that are growing very fast. If cells are growing so fast that their demand to make stuff outstrips how much ATP they're burning, that's when they flip over into this type of metabolism. So, it solves, in my mind, many of the paradoxes that have existed."

More Evidence for Senescent Cell Clearance as a Treatment for Neurodegenerative Conditions

January, 2021

Senescent cells accumulate in the brain with age, and these cells generate chronic inflammation in brain tissue. Neurodegenerative conditions such as Alzheimer's disease are known to prominently involve inflammation in the progression of pathology. At least one senolytic treatment, the combination of dasatinib and quercetin, can pass the blood-brain barrier to destroy senescent cells in the brain, and has been shown to reduce inflammation and reverse tau pathology in mouse models of Alzheimer's disease. Researchers here add more data to this subject, clearing senescent cells from the brains of aged mice, and finding that this reverses a sizable fraction of the age-related loss of cognitive function that normally takes place. At least one human trial has started up to test the use of dasatinib and quercetin to treat Alzheimer's disease; this is a very promising area of study.

Cellular senescence is characterized by an irreversible cell cycle arrest and a pro-inflammatory senescence-associated secretory phenotype (SASP), which is a major contributor to aging and age-related diseases. Clearance of senescent cells has been shown to improve brain function in mouse models of neurodegenerative diseases. However, it is still unknown whether senescent cell clearance alleviates cognitive dysfunction during the aging process.

To investigate this, we first conducted single-nuclei and single-cell RNA-seq in the hippocampus from young and aged mice. We observed an age-dependent increase in p16Ink4a senescent cells, which was more pronounced in microglia and oligodendrocyte progenitor cells and characterized by a SASP. We then aged INK-ATTAC mice, in which p16Ink4a-positive senescent cells can be genetically eliminated upon treatment with the drug AP20187 and treated them either with AP20187 or with the senolytic cocktail Dasatinib and Quercetin. We observed that both strategies resulted in a decrease in p16Ink4a exclusively in the microglial population, resulting in reduced microglial activation and reduced expression of SASP factors.

Importantly, both approaches significantly improved cognitive function in aged mice. Our data provide proof-of-concept for senolytic interventions' being a potential therapeutic avenue for alleviating age-associated cognitive impairment.

Link: <https://doi.org/10.1111/ace1.13296>

A Profile of Repair Biotechnologies, Working to End Atherosclerosis

February, 2021

Repair Biotechnologies is the company I founded with Bill Cherman a few years ago, to work on interesting projects in the rejuvenation biotechnology space. Time flies when one is busy. Our primary focus these days is the development of what we call the cholesterol degrading platform (CDP), a technology that does exactly what one would expect from the name. Localized excesses of cholesterol - and particularly toxic, altered forms of cholesterol - lie at the root of numerous serious medical conditions, and contribute to a lesser degree to many more.

Of those conditions atherosclerosis is the most important, given the vast numbers of people it kills, year in and year out, and given the inability of present approaches to therapy to do more than slow down its progression. Our view of this sort of challenge in medicine is to take the direct path, treat excess cholesterol as a form of damage, and repair that damage by removing the cholesterol. In an animal model of atherosclerosis, the cholesterol degrading platform achieved a 48% reversal of arterial obstruction by plaque following a single treatment.

"All of the greatest research programs start out with one scientist poking at something that he or she finds interesting. In this case it was the question of why mammalian cells do not routinely break down cholesterol, and instead make do with an intricate, fragile set of processes for shuttling cholesterol within cells and throughout the body. The presence of localized excesses of cholesterol in blood vessel walls is a lifespan-limiting circumstance that occurs to all of us, leading to atherosclerosis, then rupture or blockage of blood vessels that causes a stroke, heart attack, and death. Why then, do none of the cells involved in blood vessel tissue and the immune response to atherosclerosis actively break down cholesterol, but rather engage a Rube Goldberg apparatus of moving cholesterol around to try to solve the problem? The reason why we have atherosclerosis in the first place is that this machinery fails the moment that the tissue environment departs from a youthful, undamaged ideal. It is not robust at all. A more direct approach is needed."

The core mechanisms of CDP came into being due to the academic curiosity of a few "visionary and talented researchers"; once a way to safely break down excess cholesterol in cells was found and optimised, the Strategies for Engineered Negligible Senescence (SENS) community, who are focused on producing effective treatments for aging and age-related disease, became aware of these mechanisms and worked on implementing CDP. "The scientists presented their data at the first Undoing Aging conference, and Aubrey de Grey of the SENS Research Foundation later made an introduction to Repair Biotechnologies. The SENS philosophy - and the Repair Biotechnologies philosophy - is to

reverse age-related disease by repairing the damage that causes it. Excess cholesterol is clearly a form of damage. Removing it is a form of repair. CDP strikes at a root cause of atherosclerosis, and other conditions in which excess cholesterol drives pathology. That makes it very attractive to those of us who think of aging in terms of damage and think of rejuvenation in terms of repair.”

CDP is a platform technology that seeks to solve the root cause of cholesterol build-up by degrading excess, non-essential cholesterol with an entirely new, target-specific, rate-limited pathway, which the process introduces into cells. “We introduce a de novo pathway for catabolism of excess cholesterol, breaking it down into a water-soluble catabolite that leaves cells and is removed from the body fairly rapidly. Introduced into mice, the CDP pathway is safe and well-tolerated. It does not interfere with the normal cholesterol metabolism required for cellular activities. It is a very attractive basis for therapy.”

Link: <https://www.longevity.technology/repair-bios-novel-platform-and-exclusive-from-ceo/>

Modeling Age-Related Disease Risk as Accumulation of Senescent Cells

February, 2021

Researchers here find that a simple model of senescent cell accumulation, with thresholds at which disease occurs, can be made to match the observed variations in risk of most age-related diseases. It is interesting to ask just how much of degenerative aging is driven by this accumulation of senescent cells, and the senescence-associated secretory phenotype that causes inflammation and disrupts tissue function. Clearly not all of aging, but the results in animal studies suggest that senescent cells contribute a large enough fraction of the whole to be a compelling target for rejuvenation therapies. Models such as the one produced here help to flesh out the observed data from animal and human studies.

Recent work on senescent cell dynamics with age used these dynamics to explain the distribution of death times in mice and humans. It was shown that senescent cells are produced and removed with a half-life of days in young mice, but their removal rate slows down in old mice to a half-life of weeks. These data, together with longitudinal measurement of senescent cells in mice, were used to develop a stochastic model for senescent-cell production and removal, called the saturated-removal (SR) model. The SR model shows that senescent cells slow their own removal rate, which leads to wide variations between individuals in the number of senescent cells at old ages. Assuming that death occurs when senescent cells exceed a threshold, it was shown that the SR model explains the distribution of times of death.

Since senescent cells are implicated in many age-related

diseases, and since a threshold-crossing event of senescent cells in the SR model has an exponentially rising probability with age, we asked whether age-related diseases can be modeled as a threshold-crossing phenomenon in which senescent cells exceed a disease-specific threshold. To explain the drop in incidence at very old ages, we add to this model the epidemiological notion of heterogeneity, in which some people are more susceptible to the disease than others. We show that the SR model with differential susceptibility provides a model with 2 or 3 free parameters that can explain a wide range of age-related incidence curves. This includes the incidence of many types of cancer, major fibrotic diseases, and hundreds of other age-related disease states obtained from a large-scale medical record database.

This conceptual picture explains why different diseases have similar exponential rise in incidence and a drop at very old ages, based on a shared biological process, the accumulation of senescent cells. It also can be used to optimize the frequency of treatments that eliminate senescent cells, showing that even infrequent treatment starting at old age can reduce the incidence of a wide range of diseases.

Link: <https://doi.org/10.1111/ace1.13314>

Most Children Born this Century Will Live to be Centenarians if Present Trends in Longevity Continue

February, 2021

Present trends in human life expectancy were established in an era in which little to nothing was being done to target the mechanisms of aging. As of fairly recently, this is changing. There is now a growing contingent of researchers, entrepreneurs, and clinicians attempting to treat aging as a medical condition. This introduces a shift from (a) trying - and largely failing - to address the symptoms of aging, to (b) trying to control the causes of aging. This will inevitably produce far greater gains in life expectancy than those achieved in the past, but the size and timing of those gains will be hard to predict.

This is worth thinking on, when reading papers such as the one below, in which the authors project past trends into the future. Those past trends, a slow increase in life expectancy at birth, as well as remaining adult life expectancy at every age, year after year, will almost certainly not continue as-is. It will rather leap upward as the first rejuvenation therapies worthy of the name are widely deployed. But when and by how much will the numbers change?

It seems a fool's game to try to predict that outcome with any accuracy, but a great many of the world's institutions have come to depend upon good predictions of future life expectancy, perhaps lulled by the consistency of the trend to date. Consider

the massive providers of life insurance, pensions, entitlement programs, and so forth, all of which calibrate their operations to a given level of mortality and survival in later life. There will thus be some upheaval attendant to the grand success of adding a few decades to the healthy human life span in the years ahead. A changing environment tends to shake out the dead wood from the competitive economic landscape. But at the end of the day, longer healthy life spans are always an economic good. More people will be productive for longer, with lower medical costs.

Demographic perspectives on the rise of longevity

This article reviews some key strands of demographic research on past trends in human longevity and explores possible future trends in life expectancy at birth. Demographic data on age-specific mortality are used to estimate life expectancy, and validated data on exceptional life spans are used to study the maximum length of life. In the countries doing best each year, life expectancy started to increase around 1840 at a pace of almost 2.5 years per decade. This trend has continued until the present. Contrary to classical evolutionary theories of senescence and contrary to the predictions of many experts, the frontier of survival is advancing to higher ages. Furthermore, individual life spans are becoming more equal, reducing inequalities, with octogenarians and nonagenarians accounting for most deaths in countries with the highest life expectancy.

If the current pace of progress in life expectancy continues, most children born this millennium will celebrate their 100th birthday. Considerable uncertainty, however, clouds forecasts: Life expectancy and maximum life span might increase very little if at all, or longevity might rise much faster than in the past. Substantial progress has been made over the past three decades in deepening understanding of how long humans have lived and how long they might live. The social, economic, health, cultural, and political consequences of further increases in longevity are so significant that the development of more powerful methods of forecasting is a priority.

Link: <https://doi.org/10.1073/pnas.2019536118>

Economic Research on Treating Aging to Extend Healthy Longevity

February, 2021

In one sense, there is an enormous wealth of research on the economics of longer lives. This is a byproduct of the operations of sizable pensions and life insurance industries, dependent as they are on successfully predicting future trends in life span. On the other hand, outside this somewhat narrow scope, most concerned with the gain of a tenth of a year here and the loss of a tenth of a year there, there is comparatively little economic work that is directly tied to the research and advocacy communities engaged in trying

to treat aging and greatly lengthen healthy human lifespan. That will change as the longevity industry both grows and succeeds in introducing age-slowng and rejuvenating therapies into the clinic.

The paper and commentary that I point out below might be taken as a sample of what lies ahead for the economics profession. At least some economists are at present managing to convince grant-awarding bodies in their field that, yes, there is real movement towards the treatment of aging, and perhaps someone should look into how that will likely play out in markets and societies. It should come as no great surprise to the audience here that even modest gains in slowing or reversing aging have vast economic benefits when they occur across an entire population. The cost of coping with aging is vast, the cost of incapacity and lost knowledge and death due to aging equally vast. It is by far the biggest and most pressing issue that faces humanity, and now we enter an era in which we can finally start to do something about it.

Investigating an Economic Longevity Dividend

Every country around the world is set to see an increase in the share of its population aged over 65. That leads to concerns about the negative macroeconomic consequences of an ageing society. However, at the same time life expectancy trends mean we are living longer and are on average in good health for longer. That should be good news for the economy. Future economic growth depends on exploiting the opportunities a longevity dividend brings and minimising the costs of an ageing society. In 2020 the ESRC awarded Professor Andrew Scott a £1 million grant to investigate an economic longevity dividend. The research program is both empirical and theoretical and is aimed at identifying the magnitude of a longevity dividend, the channels through which it operates and the policies that can be used to maximise its impact.

Paper All's Well That Ages Well: The Economic Value of Targeting Aging

Life expectancy has increased dramatically over the last 150 years. These developments pose a number of important questions: Is it preferable to make lives healthier by compressing morbidity or longer by extending life? What are the gains from targeting aging itself, with its potential to make lives both healthier and longer? How does the value of treating aging compare to eradicating specific diseases? How will these gains evolve over time and be affected by demographic trends? We take an economic rather than biological perspective to answer these questions. Specifically, we use the Value of Statistical Life (VSL) approach to place a monetary value on the economic gains from longer life, better health, and changes in the rate at which we age.

VSL models have two distinct advantages for our purposes. Firstly, they are already used by a variety of government agencies to evaluate different policy measures and treatments. Secondly,

by modeling how economic decisions interact with changes in health and longevity, we can analyze not just the current gains to targeting aging but how these gains will evolve in the future. The results reveal a distinctive feature of age-targeting treatments. Interactions between health, longevity, economic decisions and demographics create a virtuous circle, such that the more successful society is in improving how we age the greater the economic value of further improvements.

The trillion dollar upside to longevity

The study revealed that a compression of morbidity that improves health is more valuable than further increases in life expectancy. However, in order to raise economic gains, longevity has to improve too. Slowing down aging reduces the rate at which biological damage occurs and improves both health and mortality. The authors calculated a slowdown in aging that increases life expectancy by one year is worth \$38 trillion, and for ten years \$367 trillion!

https://longevitydividend.london.edu/wp-content/uploads/2021/01/allswell_080121.pdf

Pharmacology to Target the Mechanisms of Aging is a Going Concern

March, 2021

Traditional pharmacological drug development involves (a) identifying a protein or protein interaction of interest in the body, (b) screening the small molecule libraries for a compound that affects that target, and then (c) making a better version of that small molecule: more effective, less harmful. That remains the bulk of the medical research and development industry, despite the proliferation of other approaches, including cell therapies, gene therapies, recombinant proteins, monoclonal antibodies, and so forth. There are goals that cannot be achieved by small molecules, and, as techniques improve and costs fall, gene therapies of various sorts will ultimately replace a great many small molecule therapies.

That is yet to come, however, and thus much of the first wave of the longevity industry is focused on turning out small molecule drugs that can in some way influence mechanisms of aging. This can be very promising, as in the case of senolytic drugs that cause senescent cells to self-destruct, or it can be likely of only modest benefit, as in the case of mTOR inhibitors that provoke cells into greater stress response activity. All too much of the work taking place today is of the latter category, and will probably provide, at best, similar gains in long term health and life span to those that can be achieved by exercise or the practice of calorie restriction. If we want to truly change the shape of a human life, more than this is needed.

The number of compounds that have been shown to increase longevity in preclinical models is growing exponentially: it was

approximately 300 in 2005, 1300 in 2015, and most recently to 2000 in 2020. Meanwhile, the discovery of longevity-associated genes has plateaued, following an exponential growth until approximately 2010 before transitioning to a slower growth over the last decade. There are probably many more longevity genes left, but the incentives for their discovery are reduced since most newly discovered genes now tend to eventually lead towards already known pathways.

The number of longevity companies has also doubtlessly increased dramatically, although this is harder to subjectively measure, as it is difficult to define what makes a company longevity-focused. Most of these companies deal with the hallmarks of aging, most notably oxidative stress and mitochondrial dysfunction, cellular senescence, and pathways implicated in caloric restriction, such as mTOR. The acquisition of longevity companies by big pharma, for example the purchase of Alkahest by Grifols, is also just beginning to occur. One concern is the lack of strategic diversity. It is possible that too much weight is being put on these areas despite the much broader range of potential strategies.

Recently, the field has also seen its first clinical failures, a notable rite of passage for all new fields of medicine. In 2019, ResTORbio's mTOR inhibitor RTB101 failed its Phase 3 trial for a lung disease, and Unity Biotechnology's senolytic UBX0101 failed to meet its endpoints in osteoarthritis just last year. A myriad of challenges can complicate translation, such as a lack of genetic diversity in preclinical models, pathways that are not conserved between species, and the selection of proper primary endpoints. However, the list of ongoing clinical trials is constantly growing, with active studies including COVID-19, macular degeneration, frailty, and neurodegenerative diseases. The TAME trial of metformin represents a pivotal proof-of-concept study, which may pave the way for future therapies aiming to broadly target longevity in their applications to the FDA rather than any specific disease. Interest has also been growing in off-label prescriptions and nutritional supplements.

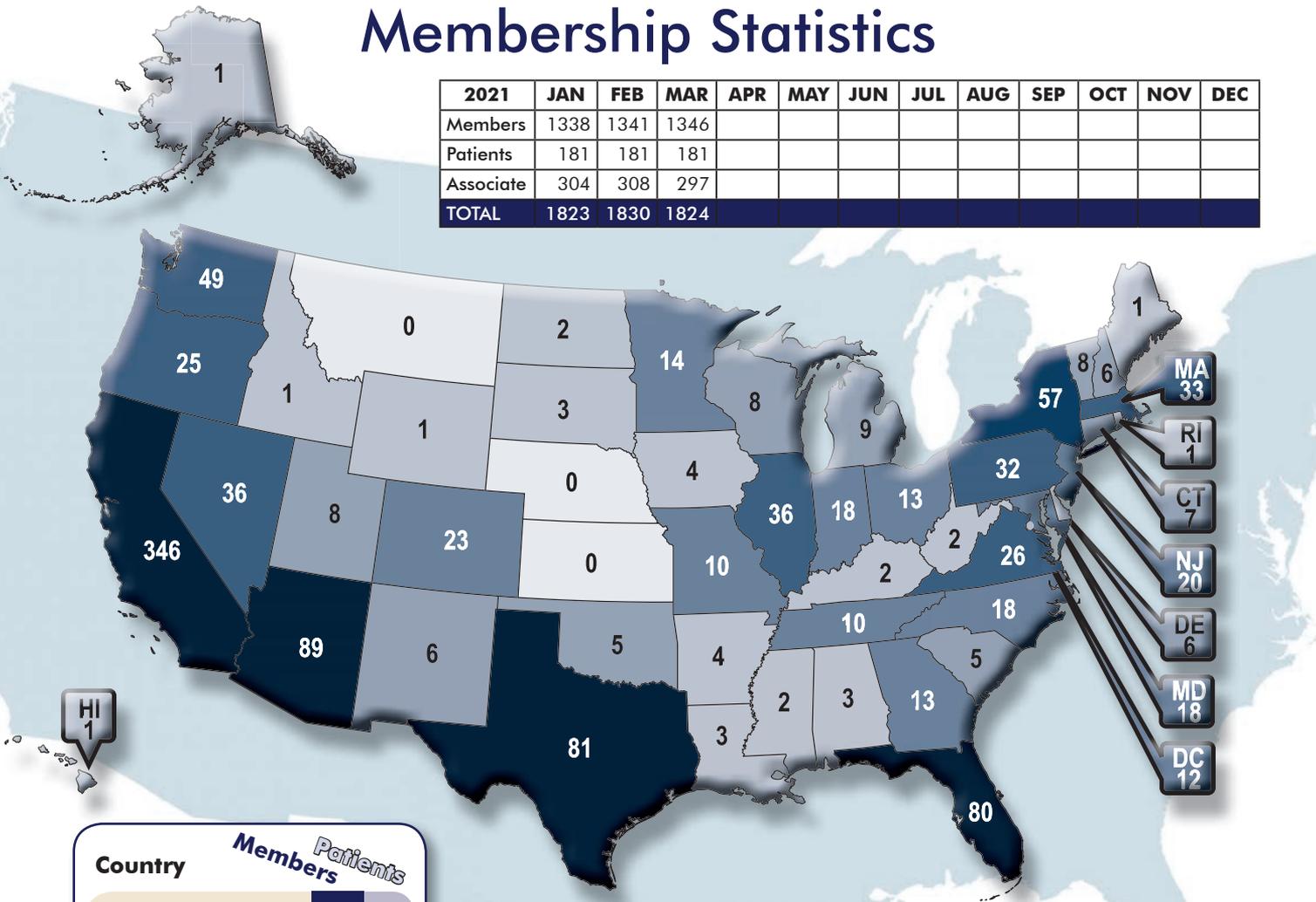
There has also been a ramping up of computer-based methods being applied to the field of longevity. Bioinformatics, machine learning, and artificial intelligence, -omics approaches, and large public databases are just beginning to be fully utilized. These techniques may someday improve our abilities to predict the outcomes of clinical trials. They also aim to identify candidate drugs and biomarkers and may eventually play a role in the application of personalized, precision medicine. When taken as a whole, these trends characterize a vibrant, growing longevity industry in its early maturation stage. There are many parallels to the early days of some fields of pharmacology that are now well established, such as cancer and heart disease.

Link: <https://www.lifespan.io/news/longevity-pharmacology-comes-of-age/>

Send email to Reason at Fight Aging!: reason@fightaging.org

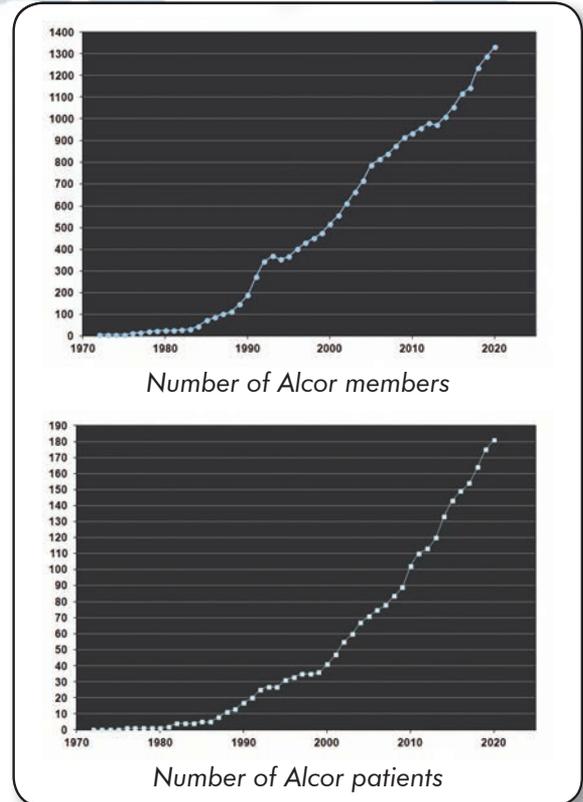
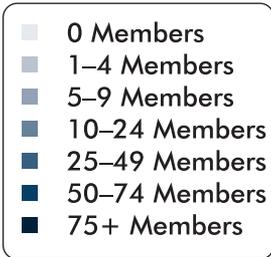
Membership Statistics

2021	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC
Members	1338	1341	1346									
Patients	181	181	181									
Associate	304	308	297									
TOTAL	1823	1830	1824									



International Members & Patients

Country	Members	Patients
Australia	11	3
Austria	1	0
Belgium	1	0
Brazil	1	0
Bulgaria	1	0
Canada	71	4
China	2	1
Croatia	0	0
Finland	1	0
France	1	1
Germany	20	0
Hong Kong	2	0
Hungary	1	0
Israel	1	1
Italy	1	0
Japan	4	0
Luxembourg	1	0
Malaysia	1	0
Mexico	5	0
Monaco	1	0
Netherlands	1	0
New Zealand	1	0
Norway	2	0
Portugal	4	1
Puerto Rico	2	0
Spain	5	1
Sweden	1	0
Switzerland	2	0
Taiwan	1	0
Thailand	3	1
United Kingdom	39	3
TOTAL	188	16





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Revival Update

Scientific Developments Supporting Revival Technologies

Reported by R. Michael Perry, Ph.D.

An Atomic Boltzmann Machine Capable of Self-Adaption

Brian Kiraly, Elze J. Knol, Werner M. J. van Weerdenburg,
Hilbert J. Kappen, and Alexander A. Khajetoorians

Nature Nanotechnology Letters, 1 February 2021, <https://www.nature.com/articles/s41565-020-00838-4>, accessed 11 Apr. 2021.

Abstract

The quest to implement machine learning algorithms in hardware has focused on combining various materials, each mimicking a computational primitive, to create device functionality. Ultimately, these piecemeal approaches limit functionality and efficiency, while complicating scaling and on-chip learning, necessitating new approaches linking physical phenomena to machine learning models. Here, we create an atomic spin system that emulates a Boltzmann machine directly in the orbital dynamics of one well-defined material system. Utilizing the concept of orbital memory based on individual cobalt atoms on black phosphorus, we fabricate the prerequisite tuneable multi-well energy landscape by gating patterned atomic ensembles using scanning tunnelling microscopy. Exploiting the anisotropic behaviour of black phosphorus, we realize plasticity with multi-valued and interlinking synapses that lead to tuneable probability distributions. Furthermore, we observe an autonomous reorganization of the synaptic weights in response to external electrical stimuli, which evolves at a different time scale compared to neural dynamics. This self-adaptive architecture paves the way for autonomous learning directly in atomic-scale machine learning hardware.

From: This ‘Quantum Brain’ Would Mimic Our Own to Speed Up AI

Shelly Fan, SingularityHub, 9 Feb. 2021, <https://singularityhub.com/2021/02/09/the-next-ai-hardware-could-be-a-quantum-brain/>, accessed 11 Apr. 2021.

Unless you’re in the lithium battery or paint business, you’re probably not familiar with cobalt. Yet according to a new paper, it may be the secret sauce for an entirely new kind of computer—

one that combines quantum mechanics with the brain’s inner workings.

The result isn’t just a computer with the ability to learn. The mechanisms that allow it to learn are directly embedded in its hardware structure—no extra AI software required. The computer model also simulates how our brains process information, using the language of neuron activity and synapses, rather than the silicon-based churning CPUs in our current laptops.

The main trick relies on the quantum spin properties of cobalt atoms. When cleverly organized into “networks,” the result is a “quantum brain” that can process data and save it inside the same network structure—similar to how our brains work. To sum up: it’s a path towards a true learning machine.

That’s great news for AI. Powerful as it is, machine learning algorithms are extremely energy-hungry. While the tech giants have massive data centers tailored to process computational needs, it’s inefficient and generates a huge carbon footprint. More troubling is when experts look ahead. Although computing prowess has doubled every year and half to two years—known colloquially as “Moore’s law”—recent observations show that it may be on its last legs.

Translation? We desperately need alternate computing methods.

“Our new idea of building a ‘quantum brain’ based on the quantum properties of materials could be the basis for a future solution for applications in AI,” said lead author Dr. Alexander Khajetoorians at Radboud University in Nijmegen, the Netherlands.

How can neuroscience, quantum mechanics, and AI mesh?

It starts with similarities between the brain and machine learning methods like deep learning. No surprise here, since the latter was loosely based on our minds. The problem comes when these algorithms are run on current computers. You see, even state-of-the-art computers process information and store them in separate structures. The CPU or GPU, by itself, can’t store data. This means that data needs to be constantly shuttled between the processing and memory units. It’s not a big deal for small things, like recognizing images, but for larger problems it rapidly slows the whole process down, while increasing energy use.

In other words, because AI mimics the brain, which has a completely alien structure to modern computers, there’s a

fundamental incompatibility. While AI algorithms can be optimized for current computers, they're likely to hit a dead end when it comes to efficiency.

Enter neuromorphic computing. It asks you to forget everything you know about computer design—chips, CPUs, memory hard drives. Instead, this type of new-age “computer” taps into the brain’s method for logging, processing, and storing information—all in one place. No data shuttling means less time and energy consumption, a win for AI and for the planet. ...

A Quantum-Logic Gate Between Distant Quantum-Network Modules

Severin Daiss, Stefan Langenfeld, Stephan Welte, Emanuele Distante, Philip Thomas, Lukas Hartung, Olivier Morin, Gerhard Rempe, Science 5 Feb. 2021

<https://science.sciencemag.org/content/371/6529/614>, accessed 11 Apr. 2021.

Abstract

The big challenge in quantum computing is to realize scalable multi-qubit systems with cross-talk-free addressability and efficient coupling of arbitrarily selected qubits. Quantum networks promise a solution by integrating smaller qubit modules to a larger computing cluster. Such a distributed architecture, however, requires the capability to execute quantum-logic gates between distant qubits. Here we experimentally realize such a gate over a distance of 60 meters. We employ an ancillary photon that we successively reflect from two remote qubit modules, followed by a heralding photon detection, which triggers a final qubit rotation. We use the gate for remote entanglement creation of all four Bell states. Our nonlocal quantum-logic gate could be extended both to multiple qubits and many modules for a tailor-made multi-qubit computing register.

From: Connecting Distant Qubits Just Brought Distributed Quantum Computing Closer

Edd Gent, SingularityHub, 08 Feb. 2021, <https://singularityhub.com/2021/02/08/connecting-distant-qubits-just-brought-distributed-quantum-computing-closer/>, accessed 11 Apr 2021.

Quantum computers could change the world, but first we need to work out how to build ones that are big enough to live up to this potential. A new breakthrough in the ability to connect distant qubits could show a way forward.

Most of the headline-grabbing progress on quantum computing so far has been led by companies like Google and IBM who are trying to build massive, cryogenically-cooled quantum supercomputers that take up entire basements.

This approach has allowed us to scale up from the handful of qubits researchers were experimenting with a decade ago to processors that are now approaching the 100-qubit mark. But this is still far fewer than what would be required to start tackling practical problems beyond the capabilities of conventional computers—the principal promise of the technology.

Significantly boosting the number of qubits in these devices faces some major engineering challenges. Processors with just tens of qubits are already the size of server racks, so finding ways to squeeze thousands or even millions of them into a reasonable amount of space while preventing them from interfering with each other is an unsolved problem.

This has prompted some to suggest we should instead create a distributed network of smaller quantum computers that can work together to simulate a larger one. The individual processing units could be much simpler, and you could side-step the cross-talk issues and space constraints because they wouldn't all need to be squeezed into the same location.

The trade-off is that coordinating a diffuse network like this would be much more complicated. To do anything useful with such a system, you need to be able to arbitrarily connect any two qubits in the network no matter how far apart they are.

Now researchers from the Max Planck Institute of Quantum Optics in Germany have taken the first tentative steps in this direction, by showing they can create a quantum logic gate made up of two qubits more than 60 meters apart.

Rather than relying on the superconducting qubits favored by industry leaders, the researchers used single rubidium atoms trapped inside optical cavities. They manipulated a property of the atoms known as “spin” to encode information into the qubits.

To create their quantum logic gate—synonymous to logic gates created by combining multiple transistors in a conventional computer—the researchers relied on a quantum phenomenon called entanglement, which Einstein famously dubbed “spooky action at a distance.”

...

In a paper published last week in *Science*, the researchers describe firing a single photon at one of their qubits, which reflects it and in the process becomes entangled with it. This photon is then carried along a 60-meter-long optical fiber to another qubit, which also reflects it and becomes entangled with it.

This creates a three-way entanglement between the two atoms and the photon, and by then measuring the photon and using the measurement as feedback to change the state of the first qubit, they were able to create a quantum logic gate with a fidelity of 85 percent.

Fast Stereolithography Printing of Large-Scale Biocompatible Hydrogel Models

Nanditha Anandakrishnan, Hang Ye, Zipeng Guo, Zhaowei Chen, Kyle I. Mentkowski, Jennifer K. Lang, Nika Rajabian, Stelios T. Andreadis, Zhen Ma, Joseph A. Spornyak, Jonathan F. Lovell, Depeng Wang, Jun Xia, Chi Zhou, Ruogang Zhao

Advanced Healthcare Materials, 15 Feb. 2021, <https://doi.org/10.1002/adhm.202002103>, accessed 11 Apr. 2021.

Abstract

Large size cell-laden hydrogel models hold great promise for tissue repair and organ transplantation, but their fabrication using 3D bioprinting is limited by the slow printing speed that can affect the part quality and the biological activity of the encapsulated cells. Here a fast hydrogel stereolithography printing (FLOAT) method is presented that allows the creation of a centimeter-sized, multiscale solid hydrogel model within minutes. Through precisely controlling the photopolymerization condition, low suction force-driven, high-velocity flow of the hydrogel prepolymer is established that supports the continuous replenishment of the prepolymer solution below the curing part and the nonstop part growth. The rapid printing of centimeter-sized hydrogel models using FLOAT is shown to significantly reduce the part deformation and cellular injury caused by the prolonged exposure to the environmental stresses in conventional 3D printing methods. Embedded vessel networks fabricated through multiscale printing allows media perfusion needed to maintain the high cellular viability and metabolic functions in the deep core of the large-sized models. The endothelialization of this vessel network allows the establishment of barrier functions. Together, these studies demonstrate a rapid 3D hydrogel printing method and represent a first step toward the fabrication of large-sized engineered tissue models.

From: Rapid 3D Printing Method Moves toward 3D-Printed Organs

Cory Nealon, *University of Buffalo News Center*, 5 Mar. 2021, <http://www.buffalo.edu/news/releases/2021/03/007.html>, accessed 9 Apr. 2021.

It looks like science fiction: A machine dips into a shallow vat of translucent yellow goo and pulls out what becomes a life-sized hand.

But the seven-second video, which is sped-up from 19 minutes, is real.

The hand, which would take six hours to create using conventional 3D printing methods, demonstrates what University at Buffalo engineers say is progress toward 3D-printed human tissue and

organs — biotechnology that could eventually save countless lives lost due to the shortage of donor organs.

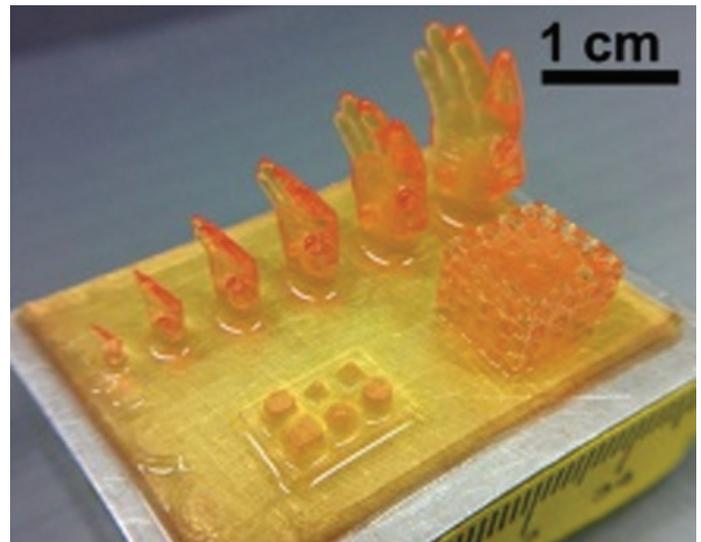
“The technology we’ve developed is 10-50 times faster than the industry standard, and it works with large sample sizes that have been very difficult to achieve previously,” says the study’s co-lead author Ruogang Zhao, PhD, associate professor of biomedical engineering.

The work is described in a study published Feb. 15 in the journal *Advanced Healthcare Materials*.

It centers on a 3D printing method called stereolithography and jelly-like materials known as hydrogels, which are used to create, among other things, diapers, contact lenses and scaffolds in tissue engineering.

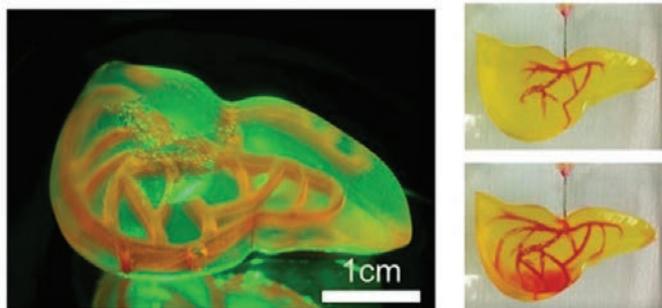
The latter application is particularly useful in 3D printing, and it’s something the research team spent a major part of its effort optimizing to achieve its incredibly fast and accurate 3D printing technique.

“Our method allows for the rapid printing of centimeter-sized hydrogel models. It significantly reduces part deformation and cellular injuries caused by the prolonged exposure to the environmental stresses you commonly see in conventional 3D printing methods,” says the study’s other co-lead author, Chi Zhou, PhD, associate professor of industrial and systems engineering.



Researchers made a series of small scale models of the 3D-printed hand, as well as other figures.
Credit: University at Buffalo.

Researchers say the method is particularly suitable for printing cells with embedded blood vessel networks, a nascent technology expected to be a central part of the production of 3D-printed human tissue and organs.



From: Sherlock Holmes' Famous Memory Trick Really Works

Yasemin Saplakoglu, *Live Science*, March 05, 2021, <https://www.livescience.com/ancient-memory-technique-creates-long-lasting-memories.html>, accessed 11 Apr. 2021.

Sherlock Holmes remembers everything by imagining that he's storing bits of information in a "memory palace," a technique that originated in ancient Greece. Now, researchers have found that this method really does work to create long-lasting memories.

Users of the mnemonic technique, called the "method of loci," mentally navigate around a familiar place, such as a path (or Holmes' palace). To remember a piece of information, you "drop" it along the path and later retrace your steps and "pick it up." For example, if you're very familiar with Central Park in New York City, you can imagine walking through it, dropping the word "book" at the Boat House, then the word "water bottle" at the next bend, then the word "space" at the fountain. When you want to remember the words, you imagine retracing your exact steps.

By training with this method, the world's best memory champions can remember inordinate amounts of information, like word lists, digit series and decks of cards, according to the study. But the World Memory Championships test only short-term memory and only a handful of studies have looked into the brain as people use this method to improve memory. ...

To evaluate the method of loci, [lead author Isabella] Wagner and her team enrolled 17 "memory athletes," or champions who were ranked among the world's top 50 in memory competitions, and 16 others that matched the athletes in characteristics such as age and intelligence. The researchers took functional magnetic resonance imaging (fMRI) scans of the participants' brains while asking them to study random words on a list. Then, the researchers presented the participants with three words at a time from the list and asked them to recall if the words were in the same order as previously studied.

In the second part of the study, they enrolled 50 participants who previously had no experience in mnemonics and trained 17 of them for six weeks to recall memories using the method of loci. The rest of the participants were in the control group (16 of them were "active controls" which meant they were trained using a different memory tactic called "working memory training," and 17 were "passive controls," meaning they weren't trained at all). They again scanned the participants' brains with fMRI as they performed the same tasks, both before and after training. The researchers also asked the participants to recall which words were on the list 20 minutes and 24 hours after their fMRI scans....

As expected, the participants showed better, longer-lasting memory after training with the method of loci than after training

Researchers also 3D-printed a human liver model that includes a vascular network. To see a video of its creation, visit: <https://www.acsu.buffalo.edu/~chizhou/liver.mp4>.
Credit: University at Buffalo.

Researchers have filed a provisional patent of the technology, and they formed a startup company, Float3D, to commercialize the technology.

Durable Memories and Efficient Neural Coding through Mnemonic Training Using the Method of Loci

I. C. Wagner, B. N. Konrad, P. Schuster, S. Weisig, D. Repantis, K. Ohla, S. Kühn, G. Fernández, A. Steiger, C. Lamm, M. Czisch, and M. Dresler, *Science Advances* 3 Mar 2021

<https://advances.sciencemag.org/content/7/10/eabc7606>, accessed 11 Apr. 2021.

Abstract

Mnemonic techniques, such as the method of loci, can powerfully boost memory. We compared memory athletes ranked among the world's top 50 in memory sports to mnemonics-naïve controls. In a second study, participants completed a 6-week memory training, working memory training, or no intervention. Behaviorally, memory training enhanced durable, longer-lasting memories. Functional magnetic resonance imaging during encoding and recognition revealed task-based activation decreases in lateral prefrontal, as well as in parahippocampal and retrosplenial cortices in both memory athletes and participants after memory training, partly associated with better performance after 4 months. This was complemented by hippocampal-neocortical coupling during consolidation, which was stronger the more durable memories participants formed. Our findings advance knowledge on how mnemonic training boosts durable memory formation through decreased task-based activation and increased consolidation thereafter. This is in line with conceptual accounts of neural efficiency and highlights a complex interplay of neural processes critical for extraordinary memory.

with the other memory technique or with no technique at all. The participants who trained with the ancient method showed a significant increase in durable memories, but not a significant change in weak memories (or short-term memories that faded after 20 minutes), compared with the control groups. ...

The team also came across something unexpected: While both the world champions and the participants were partaking in these tasks, activity in their brains declined in regions typically involved in memory processing and long-term memory, Wagner told Live Science in an email. "This was somewhat surprising to us, as better performance is typically associated with increased engagement of different brain regions," she said. ■

A Roadmap to Revival

Successful revival of cryonics patients will require three distinct technologies: (1) A cure for the disease that put the patient in a critical condition prior to cryopreservation; (2) biological or mechanical cell repair technologies that can reverse any injury associated with the cryopreservation process and long-term care at low temperatures; (3) rejuvenation biotechnologies that restore the patient to good health prior to resuscitation. OR it will require some entirely new approach such as (1) mapping the ultrastructure of cryopreserved brain tissue using nanotechnology, and (2) using this information to deduce the original structure and repairing, replicating or simulating tissue or structure in some viable form so the person "comes back."

The following is a list of landmark papers and books that reflect ongoing progress towards the revival of cryonics patients:

Jerome B. White, "**Viral-Induced Repair of Damaged Neurons with Preservation of Long-Term Information Content**," Second Annual Conference of the Cryonics Societies of America, University of Michigan at Ann Arbor, April 11-12, 1969, by J. B. White. Reprinted in *Cryonics* 35(10) (October 2014): 8-17.

Michael G. Darwin, "**The Anabolocyte: A Biological Approach to Repairing Cryoinjury**," *Life Extension Magazine* (July-August 1977):80-83. Reprinted in *Cryonics* 29(4) (4th Quarter 2008):14-17.

Gregory M. Fahy, "**A 'Realistic' Scenario for Nanotechnological Repair of the Frozen Human**

Brain," in Brian Wowk, Michael Darwin, eds., *Cryonics: Reaching for Tomorrow*, Alcor Life Extension Foundation, 1991.

Ralph C. Merkle, "**The Molecular Repair of the Brain**," *Cryonics* 15(1) (January 1994):16-31 (Part I) & *Cryonics* 15(2) (April 1994):20-32 (Part II).

Ralph C. Merkle, "**Cryonics, Cryptography, and Maximum Likelihood Estimation**," First Extropy Institute Conference, Sunnyvale CA, 1994, updated version at <http://www.merkle.com/cryo/cryptoCryo.html>.

Aubrey de Grey & Michael Rae, "**Ending Aging: The Rejuvenation Breakthroughs That Could Reverse Human Aging in Our Lifetime**." St. Martin's Press, 2007.

Robert A. Freitas Jr., "**Comprehensive Nanorobotic Control of Human Morbidity and Aging**," in Gregory M. Fahy, Michael D. West, L. Stephen Coles, and Steven B. Harris, eds, *The Future of Aging: Pathways to Human Life Extension*, Springer, New York, 2010, 685-805.

Chana Phaedra, "**Reconstructive Connectomics**," *Cryonics* 34(7) (July 2013): 26-28.

Robert A. Freitas Jr., "**The Alzheimer Protocols: A Nanorobotic Cure for Alzheimer's Disease and Related Neurodegenerative Conditions**," *IMM Report* No. 48, June 2016.

Ralph C Merkle, "**Revival of Alcor Patients**," *Cryonics*, 39(4) & 39(5) (May-June & July-August 2018): 10-19, 10-15.

What is Cryonics?

Cryonics is an attempt to preserve and protect human life, not reverse death. It is the practice of using extreme cold to attempt to preserve the life of a person who can no longer be supported by today's medicine. Will future medicine, including mature nanotechnology, have the ability to heal at the cellular and molecular levels? Can cryonics successfully carry the cryopreserved person forward through time, for however many decades or centuries might be necessary, until the cryopreservation process can be reversed and the person restored to full health? While cryonics may sound like science fiction, there is a basis for it in real science. The complete scientific story of cryonics is seldom told in media reports, leaving cryonics widely misunderstood. We invite you to reach your own conclusions.

How do I find out more?

The Alcor Life Extension Foundation is the world leader in cryonics research and technology. Alcor is a non-profit organization located in Scottsdale, Arizona, founded in 1972. Our website is one of the best sources of detailed introductory information about Alcor and cryopreservation (www.alcor.org). We also invite you to request our FREE information package on the "Free Information" section of our website. It includes:

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