Liver Transplantation: Policy and Technology

A Research Paper
in STS 4600
Presented to
The Faculty of the
School of Engineering and Applied Science
University of Virginia
In Partial Fulfillment of the Requirements for the Degree
Bachelor of Science in Biomedical Engineering

By

Sarah Zagorin

April 20, 2020

On my honor as a University student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments

Introduction

Despite advancements in organ transplant technologies that allow for more successful and efficient transplant surgeries, the gap between supply and demand for viable organs is growing (*The Need Continues to Grow - OPTN*, n.d.). This disparity in organs needed and organs available creates a challenge when deciding how available organs should be distributed amongst those in need. The current system for allocation depends on the recipient's location relative to the donor which results in geographical disparities. Consequentially, less organs go to those in lower socioeconomic classes. This pattern is especially evident in the case of liver transplants, the second most commonly transplanted organ. However, this system is not irreparable. Developing technologies carry the potential to positively impact the liver transplant system. By studying the policy surrounding liver allocation, specifically regarding the recipient's distance from the donor, I hope to discover how technologies that enable organ receivers to be farther from donors have influenced or will influence how organs are allocated. This information will help people understand the potential for organ transplantation technology to address inequalities in the current organ allocation system.

Historic Inequality in the Liver Distribution System

The disparity between supply and demand of organs continues to grow. Today, there are 112,678 people on the transplant list, awaiting an organ that will save their life. In 2019, there were 19,250 donors (*Transplant Trends*, n.d.). Policy establishing systems for organ distribution, especially livers, is frequently changing attempting to optimize the number of lives saved. Although there are specific policies for different organs, the policies share a common structure established by the Organ Procurement and Transplant Network (OPTN), a unique public-private partnership established by the Health Resources and Services Administration (HRSA) of the U.S.

Department of Health and Human Services (HHS) (*About the OPTN - OPTN*, n.d.). Currently, the United States is broken up into eleven OPTN regions. People in need of organs are placed on the waitlist within their region and are matched with organs based on a number of medical factors as well as their distance from the donor. These regions have different supply and demand for organs, resulting in certain waitlists having higher likelihoods for patients to receive organs. In 2019, there were 1,445 livers donated and transplanted in region 3, while only 331 livers were donated and transplanted in region 1. As of February 2020, 1,233 and 1,073 are registered for a liver in regions 3 and 1, respectively, demonstrating the similar demand but varying supply in the regions (Table 1) (*Regions - OPTN*, n.d.). These differences lead to people with adequate resources listing themselves in multiple regions, increasing their likelihood of receiving a lifesaving organ. In order to be listed in multiple regions, patients must be accepted to the transplant center in which they are attempting to join. Often, this requires patients to agree to conditions such as ability to come to the hospital within a certain timeframe if an organ were to become available (*Multiple Listing*, n.d.). This puts additional travel and lodging costs on the patients and their caretakers. Additionally, extended stay in the new transplant center area may be required if post-operative care cannot be performed at a facility close to the patient's home. Those without the resources to do this, or specifically, those who have Medicaid, which will not pay for transplants outside of the patients' designated region, must continue to wait for an organ, with the likely possibility of never receiving one.

***Table 1.* Comparison of Supply and Demand of Livers**

	Number of Livers Donated	**Number of People Registered for a liver donation**
Region 1	331	1,073
Region 3	1,445	1,233

The length of time between organ procurement and transplantation has been identified as one of the three major risk factors associated with the success of a liver transplant due to deteriorating quality of procured organs over time (Moore et al., 2005). Existing technologies, such as advanced preservation solutions, and developing technologies, such as machine perfusion, work to keep organs viable longer by mimicking the physiological environment of the liver, a key step in a successful transplant. By keeping the organs viable for longer, these technologies enable organs to go farther from the donor and raise questions about the reasons for keeping these OPTN regions. These technologies may enable recipients to be geographically farther from the donor, if policy surrounding liver allocation will allow for it.

How Liver Policy Changes

Liver donation is controlled by the OPTN and administered by the United Network for Organ Sharing (UNOS). UNOS is a nonprofit organization contracted by the HSS to serve for the OPTN (*About the OPTN - OPTN*, n.d.). The CEO of UNOS, Brain Shepard, states that "the transplant community shares the common goal of saving as many lives through transplantation as possible" (*Liver Distribution*, n.d.). This goal encompasses fairly sharing available organs among transplant candidates as well as optimizing distribution so that organs are given to those who are most likely to die soon, ultimately saving more lives. Policy changes are continually proposed, attempting to achieve this optimization. In order to understand how technology could influence policy and vice versa, to achieve this optimization, it is necessary to understand how the specific policy making process works for liver transplantation. Policy change begins with an OPTN committee that researches and identifies issues and then drafts a proposal. The committee then distributes the proposal to the public for comments by professionals and the general public. After revisions, the proposal is given to the OPTN Board of Directors, which votes on all policy proposals (*How We Develop Policy*, n.d.).

Methods

The proposed research question for this project is “How has and will organ transplant technology interact with liver transplant policy to address inequalities in the current liver distribution system?”. In order to answer this question, the political and technological history of liver transplants was investigated. Data was collected from the UNOS/OPTN website regarding liver transplant policy. This data includes a historical overview of liver distribution policy. Two current liver transplant technology focus areas were selected to be analyzed based on their hypothesized potential for impact on inequalities in the current liver distribution system. The potential to impact inequalities was determined by criteria related to preserving organs longer and more effectively transporting organs. Such technologies include organ delivery drones, machine perfusion, and preservation solutions. Data related to liver transplant technology was collected from peer reviewed scientific journal articles. *History of Liver Distribution Policy*

The first human liver transplant was attempted 1963, but did not ultimately end in patient survival. By 1967, the first successful liver transplant was performed, demonstrating extended patient life. Progress continued and by 1983, it was demonstrated that there was a greater survival in patients who received a liver transplant than those who did not, an important landmark for progress (Song et al., 2014). The increasing success of transplants led to an expanding pool of patients looking towards the procedure to save their life and in need of a donor organ. Even in early stages, demand for livers outnumbered supply. Liver preservation strategies were not advanced, so determining where livers were allocated was not a particular challenge. Donated livers did not have the capability of leaving the facility in which they were procured, so a complex system of allocation was not yet necessary.

Since 1983, the success of liver transplants has continued to improve. Today, liver transplants are considered a lifesaving surgery and the only option for many people suffering from End Stage Liver Disease. This success is due to improvements in surgical techniques, immunosuppression and donor selection strategies (Song et al., 2014). These technological advancements have allowed livers to leave the donor hospital, necessitating a complex system that determines who receives donated livers and in what order.

In 1984, the National Organ Transplant Act (NOTA) established the OPTN (*About the OPTN - OPTN*, n.d.). The first liver allocation policy was developed in 1987 and outlined a point system based on medical need, patient compatibility with the donated liver and waiting time, all within discrete distribution areas (*Timeline of Evolution of Liver Allocation and Distribution Policy - OPTN*, n.d.). An important moment in organ policy occurred in 2000 when the Department of Health and Human Services (HHS) implemented the final rule, which established framework for which the OPTN was to operate (*About the Final Rule - OPTN*, n.d.). The OPTN had been operating prior to the implementation of this framework, but had no official government mandated framework by which to operate. The final rule essentially states that the OPTN is to allocate and distribute resources such that the most lives are saved and the fewest organs are wasted. It stated that “neither place of residence nor place of listing shall be a major determinant of access to a transplant,” (*Timeline of Evolution of Liver Allocation and Distribution Policy - OPTN*, n.d.). In 2002, a new system for quantifying medical need was established. This took place in the form of Model End Stage Liver Disease (MELD) scores, which provide a more expansive analysis of patient need than the previous point system (Song et al., 2014).

At this point, the liver issuance policy worked in two stages, allocation and distribution. Allocation is determined based on patient MELD scores, which use a variety of medical factors to indicate the urgency of the patients' need for a new liver. Distribution is based on the region and more specific local donation service area (DSA) in which a recipient patient resides. There are 58 DSAs in the United States within the eleven OPTN regions. Livers that are medical matches for recipients are first shared within a DSA, then regionally, and then nationally (Elwir & Lake, 2016). In 2013, policy shifted towards wider sharing of organs with implementation of the Regional Share 35 and National Share 15 policies. The Regional Share 35 policy calls for primary regional sharing before local sharing for patients with MELD scores of 35 or higher (high risk of death without transplant). The National Share 15 policy requires that if there are no matches with a MELD score over 15 locally, organs are offered regionally, then nationally, before being given to a local recipient with a score under 15 (Elwir & Lake, 2016). These changes resulted in a reduction in waitlist mortality (Deshpande et al., 2017).

Current Liver Distribution Policy

On February 4th, 2020 the OPTN implemented a new policy for distribution of livers and intestinal organs, coined the Acuity Circles Model. The goal of this policy is to eliminate regions and donation service areas (DSAs) in an attempt to save more lives and provide more equitable access. This new system considers recipient urgency as well as the distance from the donor hospital to the transplant hospital. Distance between hospitals is considered in concentric circles from donor hospital at 150, 250 and 500 nautical miles.

The most urgent candidates within 500 nautical miles of the donor hospital will be considered first. Next candidates with MELD scores of 37 or higher are considered at 150, 250, then 500 miles. If no matches occur, candidates with increasingly smaller MELD scores are considered beginning in the closest concentric circle to the hospital and extending outwards.

In the event that the donor contains certain risk factors that impact the organ viability time, such as older than 70 or death by cardiorespiratory failure, the sequence of events is different. These livers are still first offered to those candidates facing imminent death within a 500 nautical mile radius. Next these livers are offered to those with a MELD score of 15 or above within the closest concentric circle, expanding outward if no matches occur (*Liver and Intestine Distribution Using Distance from Donor Hospital*, n.d.).

The Acuity Circles Model policy addresses disparity within regions. DSAs were of varying sizes, shapes and populations, which resulted in inequity of distribution within regions (*Liver and Intestine Distribution Using Distance from Donor Hospital*, n.d.). Despite the claims the OPTN has made for the projected positive impact of the new policy, the policy has received significant pushback. This policy was originally passed by the OPTN Board of Directors in December 2018 and was implemented in May 2019, but the policy quickly reverted back to the original policy because of a court order due to a lawsuit. Four transplant candidates and fourteen prominent medical centers that perform transplants filed a law suit challenging the new policy, arguing that the new policy would make it harder for medical centers outside of urban areas to receive organs and thus the policy disproportionately disadvantaged those who live in rural areas, which often contain higher rates of poverty and under-insurance (Goggin, 2020). In January of 2020, the court ruled that although the plaintiff's claim's may be true, the OPTN met the legal standard. The policy was reimplemented in February 2020.

Despite this opposition, UNOS states that the "policy was developed by transplant and donation experts, recipients and donor families and considered public comment," but much published public comment was in clear opposition to the policy changes (*Liver and Intestine Distribution Using Distance from Donor Hospital*, n.d.). Most concern was expressed regarding the size of the concentric circles surrounding the donor hospital, indicating that the circles should cover a larger area.

As previously described, the OPTN frequently updates policy in an attempt to save more lives and provide more equal access. The OPTN supports the most recent policy shift by claiming statistical models have demonstrated that this policy will “save more lives, with fewer patients dying while waiting for a liver transplant” and “the benefits of the system are projected to have similar effects across various socioeconomic groups and population types, such as urban, rural and suburban” (*New National Liver and Intestinal Organ Transplant System in Effect - OPTN*, n.d.). Time will tell the impact this policy has on equity in distribution.

Although the latest update in liver distribution policy still involves boundaries, it was a step toward eliminating geographic disparities. Previously, the liver distribution was completely dependent on arbitrary boundary lines that did not necessarily correlate to the patient’s distance from the donor. Now, the Acuity Circles Model uses boundaries directly related to the patient’s distance from the donor and uses the farthest possible distance first, translating to broader sharing of organs. For other organ distribution policies, the OPTN has released a document titled “Guidance on Effective Practices in Broader Distribution” (Hunter, n.d.). This document was written to provide guidance to regions in wider sharing of organs. It focused on the logistics of increased travel as well as communication and relationships between regions and distant hospitals. Although this document is not specific to livers, its existence represents a shift in the OPTN perspective, looking towards the future and providing a framework to shift policy as technology makes wider sharing of organs possible.

Technological Overview

Despite the drastic improvement since the first liver transplants, the field still faces a number of technological challenges. Current challenges in liver transplantation include preserving the organs after procurement and before transplant and a reliable method of transporting the livers to reach recipients that are far away. Dr. Scalea, a transplant surgeon at the University of Maryland expresses the urgency to get organs to recipients as fast as possible. When reflecting on a patient whose kidney coming from Alabama took 29 hours to arrive, Dr. Scalea expressed that “had I put that in at nine hours, the patient would probably have another several years of life.” (Zraick, 2019). This demonstrates the need for methods to get organs to patients faster and methods to maintain organ quality.

Preservation Technology

As soon as the donated liver is removed from the donor body, it begins declining in quality. Hypoxia occurs as the amount of oxygen reaching the organ declines, quickly leading to organ damage. The goal of all preservation technology is to prevent this damage thereby leading to organs that are healthier and can stay outside of the body longer. Earliest preservation technologies included cooling down the organ, to slow metabolic rate, reducing tissue’s need for oxygen thus reducing damage (Petrenko et al., 2019). In 1969, the first preservation solution was developed. Preservation solutions contain substances that allow the organ to maintain a physiological balance, preventing injury. By 1987 the University of Wisconsin developed another preservation solution, improving on the previous formulation, that successfully improved patient outcome and allowed broader sharing of organs due to the increased viability time (Cameron & Cornejo, 2015).

Today, static cold storage (SCS), in which the liver is kept in a cold preservation solution is the primary method of liver preservation. This keeps the liver viable for an average of 9 hours before the chances of successful transplantation decline (*Scientists Triple Storage Time of Human Donor Livers*, n.d.). Although this provides some time for an organ to be matched and transported, there is still room for improvement in terms of organ quality and viability time.

Alternate methods for liver preservation are currently being explored, many involving machine perfusion in which preservation solution is cycled through the liver, similar to how blood is cycled through the liver in the body. The different methods of machine perfusion (hypothermic, normothermic and subnormothermic) are categorized based on the temperature at which they occur: much below body temperature, at body temperature, and just below body temperature. Recently researchers have developed a new protocol for preserving livers, that includes hypothermic machine perfusion, that is capable of preserving human livers up to 27 hours (de Vries et al., 2019) . This protocol has not yet been used on a liver transplanted into a human, but research and development towards this goal continue. These developing technologies carry the potential for more successful liver transplants as well as broader distribution of livers.

Liver Transportation

Currently, livers can be reliably preserved 8-12 hours from the time of procurement to the time of transplantation (*How We Match Organs - UNOS*, n.d.). In some cases, livers may be transported long distances to reach their recipient. Because of the limited preservation time of livers, this often requires the use of air transport. Organs are typically transported as cargo on commercial airlines due to the expense of flying private. In some emergent cases, air ambulances are utilized in which a specialized fleet and medical crew deliver the donated organ (*Air Ambulance Transportation Services for Organ Transplant Recipients*, n.d.). As previously discussed, emerging technologies have the potential to keep livers viable longer. Extended viability opens doors for transporting organs even farther and more often, due to simple time allowance. In order to utilize this opportunity, it is necessary to have reliable, safe and effective methods of transporting organs in place.

A longitudinal study was performed in Australia analyzing the effects of plane transport on the success of liver transplants (Huang et al., 2016). Australia commonly shares organs regionally and nationally and thus livers are frequently transported by plane. This study concluded that airplane transport was associated with reduced graft survival, meaning reduced survival of the transplanted liver inside of the recipient. This association was independent from increased cold ischemia time, the time in which the liver is outside the body and in cold preservation solution, which was also associated with reduced graft survival. It was hypothesized that this reduction in graft survival could be attributed to a number of air transport environmental factors such as pressure changes (Huang et al., 2016).

This study further demonstrates the need for improvement in transportation methods. If preservations solutions continue to progress, enabling organs to withstand long travel times, the success of long-distance transplants is dependent on the ability to maintain organ quality during transport. Currently, some strides are being made towards this problem. At the University of Maryland, researchers are working towards developing drones specialized in delivering donated organs (Zraick, 2019). These drones are equipped to measure temperature, barometric pressure and vibrations to ensure the safety of the organ (Zraick, 2019). In addition to providing a fast method of transport that maintains organ quality, these drones allow doctors to precisely monitor the status of the organ and know exactly when it will be arriving. This has the potential to improve work flow and efficacy of the transplant. So far, Dr. Joseph R. Scalea and his team successfully delivered a donated kidney using one of these specialized drones. This first delivery was only three miles, transporting the kidney to a nearby hospital, but they are working towards flying longer distances. At its current state, this technology is most useful for applications such as avoiding traffic in big cities.

Technologies such as organ delivery drones provide an example of steps taken towards innovating better solutions for transporting livers for transplantation. Technologies such as these have the potential to allow organs to go farther, faster, with less disruption to the organ.

Interaction of Policy and Technology

Steady progress has continued since the 1960s in terms of both technology and policy. Technology has evolved to ensure the success of these life saving surgeries while policy has evolved to distribute precious resources effectively and fairly. In 1987 when preservation solution technology improved to the point that organs could be shared outside of the donor hospital, the first liver distribution policy was introduced. This demonstrates an instance in which policy was established in reaction to a problem. The technology was ready to save lives, so the policy was created to ensure this could occur. The policy was introduced to maximize the positive impact of technological progress on society. After 1987, the interaction between policy and technology becomes less clear. Technological development came more gradually, as did changes in policy. Policy worked towards distributing organs to save lives, arranging and rearranging methods for determining who was most in need of livers. As physicians and researchers found ways to determine who needed livers most, policy changed to reflect these new scoring systems. Policy strove towards optimizing the number of lives saved while factors, including technological capabilities of liver transplants, evolved.

The most recent liver policy update is another attempt to achieve this optimization. Current technology allows livers to be shared effectively at a distance of at least 500 nautical miles, as demonstrated by the largest radius of the Acuity Circles Model. Although this policy still includes geographic boundaries, thus patient location is still considered when distributing livers, this policy is sharing organs more broadly and laying groundwork for a system that might not consider geography as a factor. This system eliminates previous boundaries, thus expanding the network of communication between hospitals outside of DSAs and outside of regions. Effective sharing networks are important, and a limiting factor, when considering sharing organs more widely so expanding these networks will allow for an easier transition away from a geography-based system. Additionally, I see this policy as adaptable. Small changes, such as increasing the size of the concentric circles, can be made in response to technological or logistical progress that allows wider sharing as technology enables organs to travel faster and stay viable longer. Although OPTN policy update notices do not specifically cite technological improvement as a driver to change policy, there is clearly a strong and important correlation

Conclusion

Organ donation policy is a good example of the symbiotic relationship between policy and technology. Without the policy to distribute donated livers, livers would only be able to be shared in the same hospital that they were procured, significantly reducing the number of lives saved. Without the technology that makes liver transplants a lifesaving operation, a complex network of distribution would be worthless. The faster the two respond to each other, the greater societal impact each has. Policy and technology can work together to solve problems. As organs can be shared more broadly and as policy evolves, geographic based inequalities can be reduced or eliminated ensuring that everyone has a fair chance at receiving a live saving resource.

Recognizing the relationship between policy and technology is necessary step in optimizing technology to reach its full potential. This relationship not only applies to organ transplants, but exists for almost any innovative technology that carries the potential to impact the world. Learning from the examples of organ transplant can help avoid policy stunting the beneficial impact of emerging technologies.

References

About the Final Rule—OPTN. (n.d.). Retrieved April 10, 2020, from https://optn.transplant.hrsa.gov/governance/about-the-optn/final-rule/

About the OPTN - OPTN. (n.d.). Retrieved April 10, 2020, from https://optn.transplant.hrsa.gov/governance/about-the-optn/

Air Ambulance Transportation Services for Organ Transplant Recipients. (n.d.). Angel MedFlight. Retrieved April 10, 2020, from https://www.angelmedflight.com/organ-transplants

Cameron, A., & Cornejo, J. F. (2015). Organ preservation review: History of organ preservation. *Current Opinion in Organ Transplantation*, *20*(2), 146–151. https://doi.org/10.1097/MOT.0000000000000175

de Vries, R. J., Tessier, S. N., Banik, P. D., Nagpal, S., Cronin, S. E. J., Ozer, S., Hafiz, E. O. A., van Gulik, T. M., Yarmush, M. L., Markmann, J. F., Toner, M., Yeh, H., & Uygun, K. (2019). Supercooling extends preservation time of human livers. *Nature Biotechnology*, *37*(10), 1131–1136. https://doi.org/10.1038/s41587-019-0223-y

Deshpande, R., Hirose, R., & Mulligan, D. (2017). Liver allocation and distribution: Time for a change. *Current Opinion in Organ Transplantation*, *22*(2), 162–168. https://doi.org/10.1097/MOT.0000000000000397

Elwir, S., & Lake, J. (2016). Current Status of Liver Allocation in the United States. *Gastroenterology & Hepatology*, *12*(3), 166–170.

Goggin, K. (2020, January 17). *New Liver Transplant Policy Cleared to Go Despite Pending Court Battle*. https://www.courthousenews.com/new-liver-transplant-policy-cleared-to-go-despite-pending-court-battle/

How we develop policy. (n.d.). UNOS. Retrieved October 8, 2019, from https://unos.org/policy/how-we-develop-policy/

How we match organs—UNOS. (n.d.). Retrieved March 6, 2020, from https://unos.org/transplant/how-we-match-organs/

Huang, Y., MacQuillan, G., Adams, L. A., Garas, G., Collins, M., Nwaba, A., Mou, L., Bulsara, M. K., Delriviere, L., & Jeffrey, G. P. (2016). Effect of airplane transport of donor livers on post-liver transplantation survival. *World Journal of Gastroenterology*, *22*(41), 9154–9161. https://doi.org/10.3748/wjg.v22.i41.9154

Hunter, R. A. (n.d.). Guidance on Effective Practices in Broader Distribution. *OPTN/UNOS Public Comment Proposal*, 22.

Liver and Intestine Distribution Using Distance from Donor Hospital. (n.d.). 55.

Liver distribution. (n.d.). UNOS. Retrieved October 8, 2019, from https://unos.org/policy/liver-distribution/

Moore, D. E., Feurer, I. D., Speroff, T., Gorden, D. L., Wright, J. K., Chari, R. S., & Pinson, C. W. (2005). Impact of Donor, Technical, and Recipient Risk Factors on Survival and Quality of Life After Liver Transplantation. *Archives of Surgery*, *140*(3), 273–277. https://doi.org/10.1001/archsurg.140.3.273

Multiple listing. (n.d.). Transplant Living. Retrieved December 4, 2019, from https://transplantliving.org/before-the-transplant/waiting-for-your-transplant/multiple-listing/

New national liver and intestinal organ transplant system in effect—OPTN. (n.d.). Retrieved April 10, 2020, from https://optn.transplant.hrsa.gov/news/new-national-liver-and-intestinal-organ-transplant-system-in-effect/

Petrenko, A., Carnevale, M., Somov, A., Osorio, J., Rodríguez, J., Guibert, E., Fuller, B., & Froghi, F. (2019). Organ Preservation into the 2020s: The Era of Dynamic Intervention. *Transfusion Medicine and Hemotherapy*, *46*(3), 151–172. https://doi.org/10.1159/000499610

Regions—OPTN. (n.d.). Retrieved October 31, 2019, from https://optn.transplant.hrsa.gov/members/regions/

Scientists triple storage time of human donor livers: Research project develops new method to preserve human livers for transplantation. (n.d.). ScienceDaily. Retrieved April 10, 2020, from https://www.sciencedaily.com/releases/2019/09/190909193208.htm

Song, A. T. W., Avelino-Silva, V. I., Pecora, R. A. A., Pugliese, V., D'Albuquerque, L. A. C., & Abdala, E. (2014). Liver transplantation: Fifty years of experience. *World Journal of Gastroenterology : WJG*, *20*(18), 5363–5374. https://doi.org/10.3748/wjg.v20.i18.5363

The Need Continues to Grow—OPTN. (n.d.). Retrieved September 25, 2019, from https://optn.transplant.hrsa.gov/need-continues-to-grow/

Timeline of evolution of liver allocation and distribution policy—OPTN. (n.d.). Retrieved April 10, 2020, from https://optn.transplant.hrsa.gov/governance/policy-initiatives/liver-timeline/

Transplant trends. (n.d.). UNOS. Retrieved September 25, 2019, from https://unos.org/data/transplant-trends/

Zraick, K. (2019, April 30). Like 'Uber for Organs': Drone Delivers Kidney to Maryland Woman. *The New York Times*. https://www.nytimes.com/2019/04/30/health/drone-delivers-kidney.html