**Appendix 3: Data tables, FA7391 Preservation of Traumatically Amputated/Avulsed Parts**

**Characteristics of Experimental Studies, Observational Studies and Systematic Reviews**

| **First Author/Year** | **Country** | **Study Timeframe** | **Population** | **Preservation Technique** | **Surgical Intervention** | **Comparator** | **Outcome measured** | **Main findings for Preservation Technique** | **Main findings for Patient Outcomes** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Experimental animal studies** |
| Hayhurst 1974 | Australia | Dates of experiment not provided | 10 Macaque Speciosa stump-tailed monkeys; 10 index fingers surgically amputated. | 1.5 hours of warm ischemia during amputation procedure. Fingers then placed in surgical sponge, moistened with normal saline and kept at ~4°C for ~21 hours; finger allowed to return to room temperature for up to 2.5 hours for replantation. | Replantation 24 hours after amputation and cold storage, all received magnesium sulphate, persantine and aspirin.7 monkeys received heparin SQ daily. | N/A | Survival of amputated fingers; histological or angiographic studies. | Preservation for 21 hours at 4°C did not produce enough damage to preclude a reasonable chance of survival in digital replantation. | The first three amputated fingers had complete necrosis. One subject died unexpectedly with normal appearing replanted finger. One finger had bleeding and necrosis felt due to anticoagulant overdosage or trauma. The final five finger replants were successful with survival of replants at up to 35 days, patent vessels on angiograms. |
| VanGiesen 1983 | USA | Dates of experiment not provided. Followed 6 months post replantation. | 40 amputated rabbit ears | 1. Amputated, room air storage, and replanted within 1 hour2. Immersed in lactated Ringer's solution at 4°C (24 hours)3. Nonimmersed, stored by wrapping the ear in lactated Ringer's moistened sponge at 4°C (24 hours)4. Immersed in normal saline at 4°C (24 hours)5. Nonimmersed stored by wrapping the ear in a normal saline sponge at 4°C (24 hours)6. Immersed in lactated Ringer's and wrapped in a sponge at Room air (24 hours)7. Frozen, nonimmersed, and stored by wrapping the ear in a lactated Ringer's sponge at 0° to - 5°C (24 hours)8. Nonimmersed and stored by wrapping the ear in a lactated Ringer's sponge for 2 hours/room air, and 4°C for 22 hours | Replantation of the ear after 24 hours . | Mutual comparisons of different techniques. | Survival of replanted ear; surface temperature recording; histological findings at 6 months. | 1. 5/5 survived2. 5/5 survived3. 5/5 survived4. 5/5 survived5. 4/5 survived6. 0/5 survived7. 0/5 survived8. 4/5 survived | All replants failed to survive after 24 hours of storage at room temperature or minus 5°C. Two other failures were recorded: one stored at 4°C wrapped in a moistened normal saline surgical sponge, and one stored 2 hours at room temperature followed by 22 hours of storage at 4°C . Results suggest that there is no significant difference between immersing an amputated part in the solution or wrapping an amputated part in a moistened cloth during cooling for 24 hours at 4°C. No difference was shown when the amputated part is stored in either lactated Ringer's or normal saline solution at 4°C.The author suggests that the best method for preservation would be to wrap the amputated part in saline-moistened gauze and place this packet in a plastic bag to be floated in an iced saline solution. No difference among conventional methods of storage today were noted as long as the amputated part is not frozen or allowed to become normothermic for more than 2 hours. |
| **Observational human studies** |
| Li 2008 | China | August 1990 – March 2006 |  211 patients (117 males and 94 females, mean age 26.2 years (range 1-67)) with 211 complete fingertip amputations undergoing replantation surgery. | 1. Dry storage at room temperature (*n* = 84 digits)2. Dry storage at 2-6°C (*n* = 106 digits)3. Immersed in saline or ethanol (*n* = 21 digits) | Replantation of amputated fingertips. | Mutual comparisons of each intervention. | Replantation survival. | Multivariable analysis (adjusted for injury mechanism, use of a vein graft, smoking after the operation and platelet counts) showed that, compared to immersion in saline or ethanol, dry storage at room temperature was associated with increased survival rates in a non-statistically significant manner (aOR: 0.314, 95%CI [0.041-2.399], p=0.264), and that, again compared to immersion in saline or ethanol, dry storage at 2-6°C was associated with increased survival rates in a statistically significant manner (aOR: 0.028, 95%CI [0.003-0.270], p=0.002). There was no statistical difference between room- and low-temperature (2° to 6°C) preservation, suggesting that the amputated fingertip could bear longer warm ischemia because of its small size." | Binary logistic regression analysis for predictor of digit survival found that injury mechanism, platelet count, preservation of amputated part beforeadmission, vein grafting, and smoking after the operation were five independent prognostic variables that influence the survival of the replanted fingertip. |
| Chen 2017 | China | Jan 1, 2002-Dec 31, 2013 | 896 amputated fingers (average patient age 22.0±3.8 years)  | 1. Freeze-dried (n=536)2. Room temperature/dry (n=273)3. Soaking liquid (n=87)Specifics of how preservation performed not described; unclear if the preservation took place before arrival at hospital. | Replantation with 1 artery anastomosis or 2-artery anastomosis | N/A | Survival of replanted fingers. | 1. 518 (60.9%) survived vs 18 (40.0%) did not survive2. 257 (30.2%) survived vs 16 (35.6%) did not survive3. 76 (8.9%) survived vs 11 (24.4%) did not survive | 851/896 (94.98%) of amputated fingers were successfully replanted. Univariate analysis showed successful replantation correlated with ischemic time, etiology of injury, age, plane of severed finders, ways of preservation, artery reconstruction, platelet level and incidence of vascular crisis (P<0.05).  |
| Okumuş 2020 | Turkey | 2007 - 2015 | 14 patients (14 males, mean age 29.6 years, range 11-45) with work-related amputations of an upper extremity.  | All amputated parts but one arrived at hospital “in properly prepared cold ischemic conditions”. One without cooling had “appropriate” warm ischemic time. | Replantation of amputated extremity in 11/14 cases (withheld in multilevel crush). | N/A | 2-point discrimination, motor ROM, handgrip, Chen criteria for functional outcomes | “Recommended ischemia times for reliable success with replantation are 12 hours of warm and 24 hours of cold ischemia for digits, and 6 hours of warm and 12 hours of cold ischemia for major replants." The amputated part should be wrapped in a saline-moistened gauze sponge and placed in a plastic bag. The plastic bag should be sealed and placed on ice. The amputated part should not be placed directly on ice. | Overall satisfaction, recovery of flexor and extensor mobility, active motion of digits and thumb opposition, active movements of wristand elbow joints, recovery of sensitivity in the median and ulnar nerve, the ability of the surviving hand and/or forearm to performdaily works were all judged satisfactory in hand replantations. Some distal ulnar nerve motor function problems reported in three cases with replantation at the elbow. |
| Tark 1989 | Korea | June 1982 - June 1986 | 261 replantations of amputated digits and hands in 153 patients; 176 were complete amputations. | “Hypothermic” preservation (cold ischemia time was an identified factor in success of replantation). No description given of how “hypothermic preservation” was accomplished, and if it was performed before arrival to a hospital.  | Successful replantation and revascularization. | Unsuccessful replantation. | Survival of replantation. | Survival of replanted amputated parts was assessed based on a warm or cold ischemia time of ≤12 or ≥13 hours. There was no significant relationship between survival of the replant and length of ischemic time in the cold ischemia amputated parts group.Success rate of replantation within 12 hours of warm ischemia was higher than that after 13 hours of warm ischemia. | 140 of 176 (80%) complete amputations were successfully replanted. Survival of amputated parts was assessed based on a warm or cold ischemia time of ≤12 or ≥13 hours. There was no significant relationship between survival of the replant and length of ischemic time in the cold ischemia amputated parts group. Success rate of replantation within 12 hours of warm ischemia was higher than that after 13 hours of warm ischemia.Clean-cut proximal levelamputations and hypothermic preserved amputation parts had the highest survival rate. Ahigher survival rate and more satisfactory results with accelerated return of sensory function correlated with repair of both digital arteries and two veins rather than only one. |
| TheHoang 2009 | Vietnam | Sept 1999 – April 2006 | 10 male patients with complete forearm amputations, ages 14 months to 42 years. | None of the amputated arms were “properly preserved.” | Attempted replantation/revascularization. All amputations underwent replantation 'shortly after arrival" at the hospital. | N/A | Survival of replanted forearm. | Ischemia times ranged from 7 to 13 hours. One illustrative case described the amputated arm wrapped in a towel and transported with the patient 3 hours to the hospital. No prehospital storage/preservation of the amputated part was performed, beyond one case in which the arm was wrapped in a towel.  | All patients arrived at the hospital within 2 to 8 hours after injury and none of the amputated parts were properly stored. The overall survival rate of replanted limbs was 100% and the postoperative functional outcomes of replanted forearms rated from “excellent” to “fair” in 70% of the patients with an average follow-up period of 20 months. |
| Sinatro 2022 | USA | 2015-2019 | 91 patients with traumatic amputation and documented modality of preservation seen at a single tertiary center. | Prearrival "proper preservation" assessed, defined as "wrapping the part in saline soaked gauze inside a watertight bag and placing it on ice" (per ATLS guidelines). | Prearrival "proper preservation" assessed, defined as "wrapping the part in saline soaked gauze inside a watertight bag and placing it on ice" (per ATLS guidelines). | Improper prearrival preservation defined as anything other than wrapping the part in saline soaked gauze inside a watertight bag and placing it on ice. | Incidence of proper and improper prearrival preservation; replantation rate. | The majority of the patients (60/91, 65.9%) arrived without proper preservation of their amputated parts. Of 74 patients transported by EMS, only 35.1% had proper preservation of their amputated part. Only 25.5% of patients presenting from home had proper preservation of their amputated part(s). | Replantation was attempted at a significantly lower rate (n=14, 23.3%) in patients with improperly preserved parts than in those with properly preserved parts (n=18, 58.1%) (P=0.001). |
| Waikakul 1998 | Thailand | 1985-1994 | 186 patients (137 male, 39 female, ages 19 – 38, mean 28.6 +/- 6.95 y) with isolated complete upper limb amputations: 24 amputations of the palm, 75 at the wrist, 50 of the forearm, 9 disarticulations through the elbow, 28 amputations through the upper arm. | “Good preservation” defined as “cooling” without further description. | Replantation with revascularization. | N/A | Survival and function of the replanted extremity. | "Preservation of the amputated segment showed a significant effect on the outcome and was a better predictor than ischemic time." | Overall, there were 167 successful replantations and 16 failed replantations. Patients were followed for 2 years. Of 102 amputated extremities that were cooled, 3 replantations failed, 99 were successful. For "poor" preservation of the amputated part, 13 replantations failed, and 68 were successful (*P* <0.05, *Χ*2 8.14).Total ischemic time, gender and age did not seem to have an effect on results. In addition to prearrival preservation technique, the type and severity of injury were good predictors of successful re-implantation and functional outcome. |
| **Systematic reviews of human studies** |
| Huawei 2015 | China | Inception - June 10, 2014 -  | 3 studies included in meta-analysis of preservation technique and survival rate, total of 979 patients with 1755 amputated digits (no references provided in the review). | Storage in an ice bag. | Replantation of the digit. | No storage in an ice bag. | Survival rate of replanted fingers. | Cold storage improves the survival rate; specific methods used to cool the amputated part in the included studies were not detailed. | Amputated digits stored in low temperature more likely to survive than that in common temperature (OR 4.89, 95%CI 2.14-11.20, p=0.0002)There was no significant association between ischemia time ≤12 h and ≥12 h and replantation survival rate (no skeletal muscle in finger). |
| Shaterian 2018 | USA | 1985-2016 | 2 studies with 6,000-digit amputation and replantation cases (Li 2008 and Heistein 2003).Note: Heistein 2003 was excluded as an individual study from this scoping review as it did not provide any description of how prehospital cooling was accomplished and did not describe time interval between injury/cooling and replantation. | “Cold” preservationNo description was provided in this review of how or when cooling of the amputated part occurred or how long cooling took place. | Replantation of amputated digits. | “Warm” or room temperature preservation. | Replant survival. | The method of preservation was not statistically associated with replant survival (OR: 0.94 (p>0.05)).  | Meta-analysis revealed the number of venous anastomosis (0 vs. 1 vs. 2), the number of arterial anastomosis (0 vs. 1 vs. 2), and mechanism of injury (sharp versus blunt cut versus avulsion versus crush) to influence replant survival (p<0.05). The authors failed to find a significant association between survival and age, sex, zone of injury, digit number, tobacco use, ischemia time, method of preservation, and use of vein graft. The method of preservation was not statistically associated with replant survival (OR 0.94 (p>0.05)).  |
| Ma 2016 | China | 1989-2013 | 22 observational studies with 2,641 patients (aged 1-75 years) with 4,678 amputated digits in total, most of the patients suffered from guillotine, avulsion, and crush of their digits. Studies conducted in Brazil, China, Yugoslavia, Korea, USA, Japan, Singapore, Italy and India. | Cold (“ice”) preservation. | Digital replantation.  | Compression bandage. | Survival of replanted digit | Meta-analysis of survival rates suggested that cold preservation is associated with better replantation survival rates than emergency compression bandaging (OR 4.89, 95% CI [2.14, 11.20], P = 0.0002). | Gender and ischemia time had no significant influence on the survival rate of amputation replantation(P>0.05). Age, injured hand, injury type, zone, and the method of preservation the amputated digit significantlyinfluence the survival rate of digital replantation (P<0.05). |