Shifting the focus in the legal analysis of the first MST case

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INTRODUCTION

In Mitochondrial Replacement Techniques and Mexico’s Rule of Law: On the Legality of the First Maternal Spindle Transfer Case (henceforth MRTs and Mexico’s Rule of Law), Palacios-González and Mediana-Arellano insightfully examine the legality of two distinct MRTs, pronuclear transfer (PNT) and maternal spindle transfer (MST), paying particular attention to this last one, since recently it was successfully carried out at the New Hope Fertility Clinic, which has offices both in Mexico and New York.¹ They conclude that, within the current Mexican legal context, performing this sort of procedures can have legal consequences both at a federal and state level. At a federal level, they claim that these procedures can imply the violation of article 56 of the Regulations for the General Health Law on Health Research, which allows for the use of such techniques, only ‘to solve sterility problems that cannot be solved otherwise’ (Palacios-González and Mediana-Arellano 2017: p.15). Likewise, the use of MRTs could breach ‘regulations related to research on human beings’ (p.23). Within the legal context of the state of Jalisco, where parts the MST procedure were believed to have been conducted, ‘the intentional destruction of human embryos in vitro could be prosecuted under criminal charges as homicide, and in the State of Mexico City PNT is prohibited when a would-be-enuclated embryo is created for a non-reproductive end’ (p.23).

Their paper explores the legal status of MRTs in the USA and the UK, the biomedical aspects of both mitochondrial DNA diseases and the MRTs, and Mexico’s legal system. They offer an overview of the law and regulations’ hierarchy, from local and federal laws to international treaties, highlighting those aspects that are related to MRTs. The paper offers a clear map to help us find our way through the Mexican legal framework in order to identify the different laws and articles where there are elements that make reference,

¹ John J. Zhang et al., Live Birth Derived From Oocyte Spindle Transfer to Prevent Mitochondrial Disease, 34 REPROD. BIOMED. ONLINE 361–368 (2017). https://doi.org/10.1016/j.rbmo.2017.01.013 (accessed July 4, 2017).
usually indirectly (i.e. under interpretation), to aspects that can pertain to MRTs. The paper’s clarity in laying out this legal context makes it very accessible, even for those without legal training or unfamiliar with the Mexican context. The paper’s framework, confined to a legal perspective, is clearly set out from the onset, as are its justification and limitations. As a justification they express the need for scholarly work of this sort to contribute to Mexico’s current and long ongoing attempts to establish a specific regulation for assisted reproduction. Under their optic, Dr. Zhang’s ‘actions have affected the assisted reproduction debate in Mexico’. Although this has not been yet the case, his actions do serve as a useful example with which to think about the implications of Mexico’s current rule of law and what needs to be thought about in order to generate an applicable and just regulation.

With this in mind, I wish to add to this paper’s analysis by looking at MRTs from the science and technology studies (STS) perspective. What does this perspective entail? First, it means situating the issue in its particular context, in this case it would be addressing the current MRT and mt disease scenario in Mexico. Second, it asks for a critical use of biomedical information and an inclusion of other sources of knowledge such as ethics, philosophy, and the social sciences. Third, it asks for an analysis of the terms used, such as MRTs, mitochondria, infertility, and embryo. Finally, an STS perspective looks for the analytical silences, for the hidden distributions of power, for the untold narratives, because in the end, all of these become relevant in practice. These analytical silences can affect the way legislation is constructed and enacted because they create gaps overriding the complexity of the issue, turn important actors invisible, reproduce mainstream discussions which need to be critically reframed, and help depict technologies as unproblematic.

**SITUATING MRTs IN MEXICO**

Law makers tend to look at the local and international context in search for arguments in favor or against a particular regulation. For example, many of the over 20 law proposals presented by the Mexican parliament mention the incidence of infertility as a way to prove the urgency of this regulation. Similarly, during the debates held in the UK, one argument that was used in favor of approving MRT was the number of people affected with this disease and the savings these would imply for the National Health Service. In these narratives, the academics and institutions involved in MRT research were also frequently mentioned. However, when it comes to mitochondrial diseases in Mexico, available data are scarce. According to Francisco Montiel Sosa, a researcher at the UNAM who works on diagnostics of mt diseases, very few patients in Mexico are diagnosed with mt diseases. There are two other research groups engaged in this area: one is mapping the mitochondrial genome of the amerindian population (a team lead by Dr. Lorena Sofia Orozco Orozco at the National Genomic Institute, INMEGEN) and the other is looking for a cure using synthetic biology (a team led by Dr. Diego

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2 Cathy Herbrand, *Mitochondrial Replacement Techniques: Who are the Potential Users and Will They Benefit?* *Bioethics* 46–54 (2017). https://doi.org/10.1111/bioe.12311 (accessed July 4, 2017).

3 Sandra P. González-Santos, *The Sociocultural Aspects of Assisted Reproduction in Mexico* (doctoral) (2011). University of Sussex. http://sro.sussex.ac.uk/7081/ (accessed July 4, 2017).

4 Those who are present with mitochondrial encephalomyopathy, lactic acidosis and stroke like episodes (MELAS). Boletín UNAM-DGCS-748, Ciudad Universitaria. 06:00 hs. 29 de diciembre de 2015 http://www.dgcs.unam.mx/boletin/bdboletin/2015_748.html (accessed July 4, 2017).
González Halphen at the Mexican National Autonomous University, UNAM). All this suggest that these conditions are still not relevant within the Mexican biomedical arena.

Many of these law proposals convey a sense of unease regarding the possibility of manipulating gametes and embryos, mostly due to the social, ethical, juridical, and biomedical implications that these entities carry. They also worry that using ARTs for purposes other than aiding infertile couples might open the possibility of affecting the reproductive and evolutionary process of humanity. Thus, they consider that issues concerning assisted reproduction should no longer be a private problem, but a public issue that should be dealt with at a social and state level. 5

OPENING THE UMBRELLA

One prominent interest within the STS perspective is to question the terminology that is commonly used within scientific argumentation, in order to see what these terms highlight, what they silence, and how they shape our understanding of the world. By unpacking key terms, we are able to see the different actors and relationships involved. This, I suggest, is crucial for an in-depth analysis and reflection of how a particular technology or service can be normed and regulated. 6 In this section, I suggest opening the label MRT, an umbrella term that encompasses three germ line modifying techniques: ooplasmic or cytoplasm transfer (OT), PNT, and MST or spindle nuclear transfer. Using the umbrella term helps silence each technique’s particular history, intended purpose, and technological and biological implications; it inaccurately suggests that what is being replaced is the mitochondria, 7 and it fails to highlight that the mitochondria are not the only thing involved.

In all three cases, a full egg is needed from a donor, not just her mitochondria. Focusing only on the mitochondria distracts our attention from the choreography that has to take place for these procedures to occur. Flipping the focus to look at this as an egg donation and not a mitochondrial donation helps us remember that the donor has to go through ovarian stimulation and egg retrieval, helps us recognize that we need to think about how this role is going to be regulated, and lets us acknowledge that, particularly in these cases, the donor cannot be genetically related to the intended mother because mitochondria are inherited via the maternal line. Hence, by invisibilizing the donor, this analytical silence hides important philosophical, ethical, and regulatory questions that emerge in practice.

These techniques require more than the mitochondria. In OT, between 5% and 15% of ooplasm from a donor egg is transferred to the recipient egg, 8 which includes other ‘potentially beneficial ooplasmic components from donor oocytes’. 9 In PNT and

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5 For an overview of the social and cultural aspects of ARTs in Mexico, see González-Santos, 2011 op cit
6 Françoise Baylis, Human Nuclear Genome Transfer (So-Called Mitochondrial Replacement): Clearing the Underbrush, 31 BIOETHICS 7–19 (2017). https://doi.org/10.1111/bioe.12309 (accessed July 4, 2017).
7 Erica Haines & Ken Taylor, Rendered Invisible? The Absent Presence of Egg Providers in U.K. Debates on the Acceptability of Research and Therapy for Mitochondrial Disease, 33 MONASH BIOETH REV. 360–378, 364–365 (2015).
8 Jacques Cohen, Birth of Infant After Transfer of Anucleate Donor Oocyte Cytoplasm into Recipient Eggs, 350 THE LANCET 186–187 (1997). https://doi.org/10.1016/S0140-6736(05)62353-7 (accessed July 4, 2017).
9 Jason A. Barratt et al., Mitochondria in Human Offspring Derived From Ooplasmic Transplantation: Brief Communication, 16 HUM. REPROD. 513–516 (2001). https://doi.org/10.1093/humrep/16.3.513 (accessed July 4, 2017).
Shifting the focus

MST, the donor egg provides the entire cell structure, including its organelles; only the nucleus is discarded.\textsuperscript{10} The donated egg is the structure into which the intended mother’s nuclear DNA will be inserted. Therefore, the donor’s cell structure and functioning is crucial for either of these procedures to be successful; hence, when talking about MST, it would be more accurate to say the donor is donating an enucleated egg. Calling this technique ‘nuclear transfer’ equally blurs the role played out by the entire cell structure of the donated egg.

Within the context of MRTs, the discussion has emphasized that mitochondria have 37 genes, accounting for 0.1% of the total DNA, while nuclear DNA accounts for the 99.9% and is responsible for identity and phenotype.\textsuperscript{11} However, within this 0.1% lies the possibility of living a healthy life, or living and dying young and in much distress. Hence, these 37 genes are quite important in giving a particular quality of life to the person, but because identity and physical appearance is described as related to the nuclear DNA, the importance of mtDNA is downplayed, in turn downplaying the role of the donor, and of this procedure as a germ line modifying technology.\textsuperscript{12} On the one hand, MRTs are justified within a world view where kinship is necessarily genetic (otherwise adoption, ova donation or embryo donation would be less problematic and would also achieve the goal of having a healthy baby). On the other hand, genetic links can be tinkered at certain ends because, according to this narrative, not all genes are equal in the kinship and identity narrative: mtDNA is less important for identity, kinship, and phenotype than nuclear DNA. This makes accepting MRT less problematic than egg donation, embryo donation, or even adoption, and it allows for the egg donor to remain anonymous.\textsuperscript{13} Furthermore, because mtDNA is described as having fewer genes and mostly involved in the production of energy, it is considered less problematic to manipulate or modify it.

Opening the umbrella also allows us to see each technique’s particular history of success and failure. Both OT and PNT are techniques that have been used and reported before.\textsuperscript{14} In both cases, the outcomes lead to a banning of the use of these techniques in the countries where they were first carried out (OT was banned in the USA and PNT was banned in China). Even when OT and PNT have been used before, all MRTs are still in an experimental stage; thus, they should be treated as such, particularly since they are germ line modifying techniques.

RETHINKING TERMINOLOGY

The current legislation falls short in their definitions of terms such as embryo, conception, and infertility. These shortcomings need to be addressed, since many of the debates surrounding ARTs regulation are precisely concerning them. Let’s begin with the

\textsuperscript{10} Lyndsey Craven, Mitochondrial DNA Disease: New Options for Prevention 20 HUM. MOL. GENET. R168–R174 (2011). https://doi.org/10.1093/hmg/ddr373 (accessed July 4, 2017).

\textsuperscript{11} S. Matthew Liao, Do Mitochondrial Replacement Techniques Affect Qualitative or Numerical Identity? 31 BIOETHICS 20–26 (2017). https://doi.org/10.1111/bioe.12308 (accessed July 4, 2017).

\textsuperscript{12} John B. Appleby et al., The Ethics of Mitochondrial Replacement, 31 BIOETHICS 2–6 (2017). https://doi.org/10.1111/bioe.12313 (accessed July 4, 2017).

\textsuperscript{13} Rosa J. Castro, Mitochondrial Replacement Therapy: the UK and US Regulatory Landscapes, 3 J. L. & BIOSCL 726–735 (2016). https://doi.org/10.1093/jlb/lsw051 (accessed July 4, 2017).

\textsuperscript{14} See Barritt et al. 2001 for an overview of the different OT procedures carried out between the late 1990s and 2000 and see Zhang et al. 2016 for his report on his attempts with PNT in 2003.
embryo. Mexico’s General Health Law defines embryo as ‘the product of conception from the moment of it, and until the end of the twelfth gestational week’.15 This definition does not account for the new type of embryos that emerge within ARTs. These new embryos are implicated in different networks of relations and subject to different actions and possibilities.16 In most cases, ARTs are dealing with in vitro embryos, which are created in the laboratory, outside the human body, subject to human managing (they need to be taken care of by the clinic’s staff), and if they are going to become a child, they need to be transferred into a woman’s womb for them to implant and give way to pregnancy. Obviously, yet importantly, to access an in vitro embryo you do not have to go through the woman’s body; it is independent from it and dependent on the laboratory. Because they are in the lab, in vitro embryos that are unsuitable for pregnancy but suitable for other things (such as research) can be accessed without having to intervene the woman’s body. All this establishes the in vitro embryo in a relational state with an array of actors and possibilities that the in vivo embryo (which is created within the body of the woman) lacks. Therefore, considering these differences should be central to these legal and regulatory debates, for example, when discussing abortion. In vitro embryos cannot be aborted because they were never implanted; legislation concerning abortion is not applicable to in vitro embryos.

There are other cases in which there is need for term precision, due to the new diagnostic categories and therapeutic possibilities that ARTs have created. These techniques have fragmented processes that previously were one and allowed us to think about health conditions in other ways. For example, within ART, fertilization (the fusion of the egg and sperm’s nucleus, which can occur in vitro), conception (when the embryo has implanted, which has to be in vivo), and gestation (the development of the embryo up to fetus, also necessarily in vivo) are three distinct moments that point toward different diagnosis and therapeutics when unsuccessful. Similarly, infertility tends to be defined as ‘failure to achieve a clinical pregnancy after 12 months of regular unprotected sexual intercourse’ (Palacios-González & Medina-Arellano, 2017). This definition does not indicate why pregnancy is not achieved. It can be due to an impossibility for the egg and sperm fertilization (primary infertility), while in other cases it might be because the embryo does not implant (secondary infertility), and yet another case because there are repetitive miscarriages. All these cases can lead to not achieving pregnancy after 12 months of unprotected sexual intercourse. Proposals, debates, and reflections on regulating these matters needs to address these distinct cases and situations. As a final point, there is need to understand how pregnancy will be determined, will it be by blood tests, ultrasound images, hearing the fetus’ heartbeat or other?

CONCLUSIONS

MRTs speak of a time when western culture is prioritizing certain forms of genetic links as the main form of kinship bonds, but more interesting for this discussion, these technologies are an example of how social structures such as the legal system are struggling

15 César Palacios-González & María de Jesús Medina-Arellano, Mitochondrial replacement techniques and Mexico’s rule of law: on the legality of the first maternal spindle transfer case, 4(1) J. LAW BIOSCI. 50–69 (2017).
16 Sandra P. González-Santos, Las múltiples configuraciones de un bioartoefacto: el embrión en vitro. In APROXIMACIONES INTERDISCIPLINARIAS A LA BIOARTEFACTUALIDAD (Jorge E. Linares & Elena Arriaga Coord, UNAM 2016).
to address the issues that emerge when ARTs are used, how we are experimenting with words to refer to many of the elements involved (as shown with the term embryo), and how we are still in the process of creating many of the sociocultural figures that emerge from these interactions (for example, the case with the donor).

Palacios-González and Medina-Arellano offered an interesting analysis regarding one way of interpreting how Mexico’s current rule of law can consider MRT. With this comment, I aimed at contributing to their analysis by addressing some of their analytical silences, by opening up some of the concepts they use, and by shifting some of their perspectives in order to flip the questions they were posing.