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Short Communication

The Invasion of Zika Virus into Rio De Janeiro and Fortaleza, Brazil, Inside Out or Outside In?

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Abstract

Zika virus (ZIKAV) is a global emerging infectious disease transmitted by mosquitoes, blood and through sex. The disease is devastating to unborn children, children born with microcephaly, and their families. The Bioagent Transport and Environmental Modeling System (BioTEMS) has been used to model biological agents with potential for use as weapons of mass destruction as well as other infectious diseases and to optimize surveillance sites of these pathogens. Recently BioTEMS has been used to model ZIKAV invasion in Miami and Tampa, Florida, USA. Several models have been developed to identify the possible geographic range of ZIKAV and competent vector species, particularly *Aedes aegypti* and *Ae. albopictus*. Sometimes these models present conflicting results to how ZIKAV first invades and then spreads in a region. BioTEMS was used to analyze the movement of ZIKAV in two cities in Brazil, Rio de Janeiro and Fortaleza and compare two published models. BioTEMS identified the source of invasion in the port areas in Rio de Janeiro and Fortaleza and spreading outward. There appear to have been multiple invasions of ZIKAV into Brazil through ports with subsequent spreading outward from the sources of introduction.

ABBREVIATIONS

ZIKAV: Zika Virus; BioTEMS: Bioagent Transport and Environmental Modeling System; TIGER: Transport Introduction Gap Escalade Residence and Recruitment; IMM: Integrated Mosquito Management

INTRODUCTION

Zika virus (ZIKAV) was first isolated in 1947 from a rhesus macaque monkey and in 1948 from *Aedes africanus* from cages placed on a tower in the Zika Forest near Lake Victoria, Uganda [1]. The Zika Forest is a tropical forest, now surrounded by pastures and with small hamlets where research continues on vector-borne diseases in even using the same tower (Figure 1). However, ZIKAV is no longer restricted to transmission of *Ae. africanus* in the tropical forest ecosystem in Africa. Several *Aedes* species have now been implicated in transmission of ZIKAV to humans in urban habitats where the poor are particularly at risk and is spreading globally [2]. Establishing patterns of invasion of vectors and vector-borne diseases into new geographic areas is critical for protecting the public health and naïve human populations. Models have been developed in order to identify the nature and spread of ZIKAV in geographic regions [3]. For example, the predictive map developed for *Ae. aegypti* and *Ae. albopictus* globally has a resolution of 5 km [4]. The principle factor responsible for the introduction of disease vectors is air and ship transport [5,6]. Public health officials at the local level would benefit from higher resolution maps and information concerning sites of possible invasion of ZIKAV infected mosquitoes or humans and sites for surveillance and control to prevent the establishment of ZIKAV within a community. Where the mosquito and arbovirus may spread is also of import to public health officials. Once introduced into an area, the invasive mosquito species can spread rapidly across regions through ground transport [7-9]. In addition to the import of infected mosquitoes, introduction of ZIKAV into the a new geographic area can occur when local mosquitoes bite infected travelers and become infected or when people become infected through sex or contaminated blood [10,11].

Brazil provides a critical model of the invasion of ZIKAV because of its modern medical and public health system, epidemiologic tracking and rapid reaction to the spread of ZIKAV. ZIKAV was first detected in Brazil in May of 2015 [12].

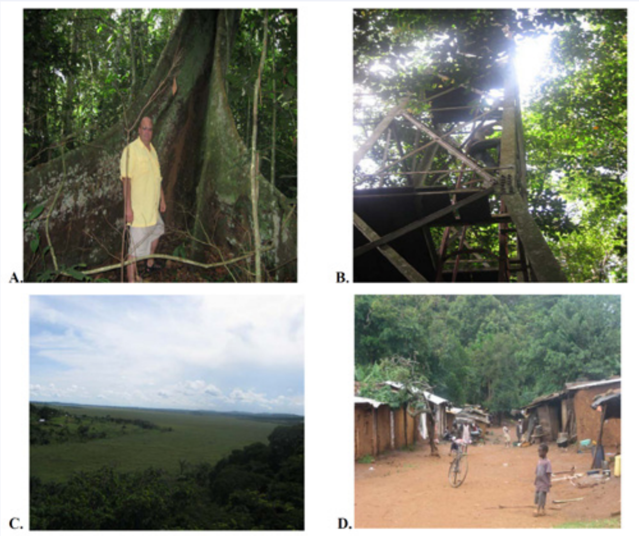

Figure 1 Conducting habitat survey in Zika Forest A. Prof Tom Kollars, B. son Jason Kollars climbing Zika Forest Tower, C. Overlook of area from tower and D. Poor hamlet near Zika Forest; courtesy Dr. Louis Mukwaya, Uganda Virus Institute:

There is controversy of how and when ZIKAV entered Rio de Janeiro, whether it spread from the north then southward into Rio de Janeiro or whether it was introduced originally in Rio, during a separate event [13,14]. The BioTEMS model was used to determine the likelihood of ZIKAV invading through the air or sea ports of Rio de Janeiro test the conclusions of these two studies, and to provide local public health officials information helpful in conducting Zika surveillance and mosquito control and testing.

MATERIALS AND METHODS

ArcGIS geospatial analysis software, Statistica software and Bioagent Transport and Environmental Modeling System (BioTEMS) were used to analyze geographic information and conduct data analysis. BioTEMS has been used for modeling biological weapons defense and infectious diseases in several countries [15]. The BioTEMS TIGER model was developed to assist in identifying areas at highest risk for invasive mosquito species and pathogens and to optimize surveillance and control efforts [16]. Transport- identifies the point of origin, method and rate of transport to a locality. Introduction- the point or area of initial introduction/immigration of species or haplo types and preliminary spread into a locality. Gap- determines the area where vector/pathogen infiltrates and initially spreads once it has gained a foothold. Escalade- incorporates abiotic and biotic factors as possible resistance to invasion. Residence and recruitment - incorporates factors and area where vector/pathogen adds to genetic diversity or becomes endemic and recruits con-specifics/haplo types. Ecological niche and dynamic change modeling are often used to predict the potential for invasion of species and were utilized in BioTEMS to predict invasion of ZIKAV in infected mosquitoes [17,18]. The BioTEMS model incorporated ecological niche and dynamic change modeling to identify areas at risk for invasion by ZIKAV and provide information for integrated mosquito management in Miami and Tampa, Florida, USA [19].

Two cities were evaluated for invasion by ZIKAV, Fortaleza and Rio de Janeiro (Figure 2). The output from BioTEMS was compared to data previously published by [13,14]. Brasil focused their research in Rio de Janeiro and Zinszer evaluated the spread of ZIKAV throughout Brazil; however, the two studies contradict one another, indicating opposite directions of invasion by ZIKAV into Rio de Janeiro. BioTEMS was used to elucidate which model was more accurate in determining direction of invasion by ZIKAV into Rio de Janeiro and to evaluate the model produced for northern Brazil proposed by [14]. The case reports in Rio were overlaid against the BioTEMS model output to determine the accuracy of each group's model. Areas at risk of Zika virus and IMM zones were developed based on the BioTEMS TIGER model should Zika virus be introduced through ports. BioTEMS and ArcGIS were used to produce output into Google® Earth.

RESULTS AND DISCUSSION

The BioTEMS TIGER model prediction for the risk of ZIKAV falls within areas of previously published assessments of geographic distribution and potential spread of the virus [20,3]. The BioTEMS TIGER model captured all confirmed local cases identified by [13] within the Invasion and Gap zones (Figure 3). However, unlike these other models BioTEMS includes origin of introduction, high risk zones and identifies areas where ZIKAV will likely spread at the local level. High risk zones are defined as an area likely to be invaded or to have already been invaded by infected mosquitoes or to have localized transmission. The Gap zone includes areas where ZIKAV will spread through infected mosquitoes. BioTEMS predicted the point of origin to be the port area (both air and maritime). The town of Niteroi, located on the west side of Guanabara Bay across from Rio de Janeiro, also seems to have been invaded through the port area, possibly by ship. The ZIKAV cases identified by [13] also fall along the direction of the spread of ZIKAV identified by BioTEMS on both sides of the bay. This is opposite of the direction of ZIKAV introduction into Rio de Janeiro posited by [14,13] detected ZIKAV RNA by RtPCR of

Figure 2 Location of the port cities of Fortaleza and Rio de Janeiro, Brazil.

patient serum in Rio de Janeiro and determined the ZIKAV cases in Rio pre-dated those in the north. Self-reported symptomatic cases were also identified as early as January, 2015 in Rio by [14]. The BioTEMS model supports and the evidence presented by Brasil et al. 2016 indicates that ZIKAV entered Rio de Janeiro in a separate event from northern Brazil. The model produced by [14] for the area of Fortaleza matches that of BioTEMS, both show a southerly direction of geographic spread of ZIKAV. BioTEMS indicates the marine or airport as the source of invasion (Figure 4). It is critical that public health authorities have information to prioritize areas in order to develop and deploy an adequate IMM plan, which incorporates vector control, public awareness and mosquito/virus testing. BioTEMS modeled the point of origin of ZIKAV introduction as the port areas in both cities, predicted the areas at highest risk for human ZIKAV cases, and the most likely direction of invasion and route of spread into the Gap area.

There is sometimes confusion as to how ZIKAV invades a new geographic area, whether through invasion of an infected mosquito or through importation by an infected human. There is absolutely no reason to rule out either of these possibilities as they are both viable. There is sometimes the failure of public health officials to recognize these two possibilities. For example, in a recent CBS 60 Minutes broadcast, Dr. Anthony Fauci (the head of infectious diseases at the National Institutes of Health) stated, “The mosquito didn’t fly from Rio de Janeiro to Florida. The mosquito flies 500 feet in a lifetime. It’s the people who travel” [21]. This ignores hundreds of years of examples of vector mosquitoes being introduced into new geographic areas. For example, *Ae. aegypti* and *Ae. albopictus*, are both invasive species in the Americas, demonstrably arriving by ship. Seaports play a critical role in the invasion of *Aedes*, this includes recruitment of new haplo types [22]. The possible invasion of arboviruses through ports, both aviation and maritime, is not a new concept

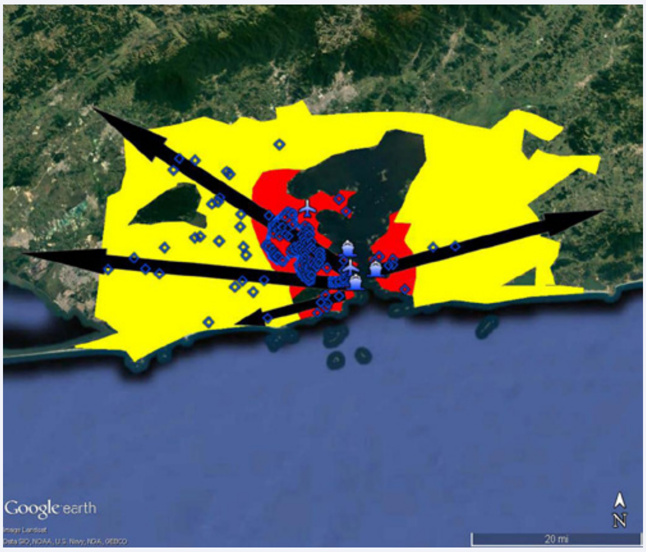

Figure 3 Areas in Rio De Janeiro first introduced and invaded by ZIKAV (red) and gap infiltration of ZIKAV into mosquito and human populations. Black arrows represent likely movement of Zika virus if brought in through port area. Blue Diamonds represent human ZIKAV cases [13].

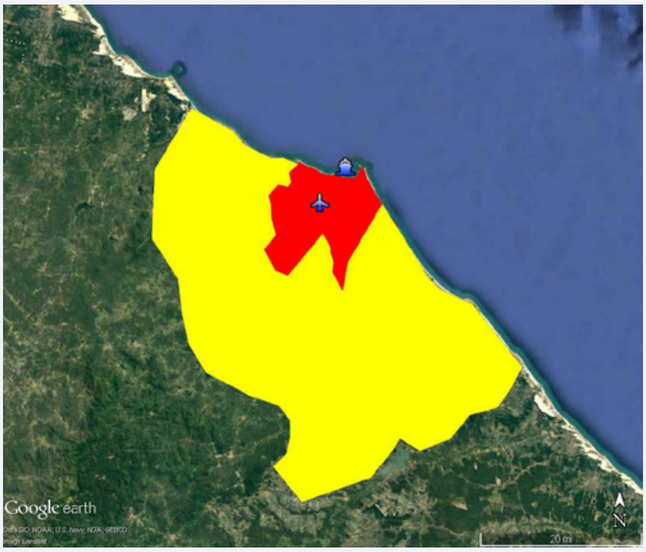

Figure 4 BioTEMS predicted areas of ZIKAV introduction (red) and gap infiltration (yellow) in Fortaleza, northern Brazil.

[23]. Focusing control and surveillance efforts primarily on travelers and not including ports of entry does a disservice to the population to whom public health officials are charged to protect. For example, if Miami had in place an active ZIKAV surveillance system for mosquitoes in the port area, the chance of finding an infected mosquito would have been increased and IMM could have been initiated sooner.

CONCLUSION

In conclusion, the BioTEMS model for identifies at least two invasion events of ZIKAV into Brazil. BioTEMS corroborates the proposal by [13] that invasion of ZIKAV occurred in Rio before the northern area of Brazil and it predicts the virus and movement through the mosquito population spread inward to outward. BioTEMS also corroborates the movement of ZIKAV through the port city of Fortaleza in the north and movement in a southerly direction as suggested by [14]. Public health officials should be cautious in making assumptions and consider implementing ZIKAV surveillance in both human and mosquito populations, particularly around air and marine ports. In other countries not yet invaded by ZIKAV, integrated mosquito management plans should be put into place before the virus arrives ashore.

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