Int. J. Production Economics 140 (2012) 865–874

Contents lists available at SciVerse ScienceDirect

Int. J. Production Economics

journal homepage: www.elsevier.com/locate/ijpe

Medical nuclear supply chain design: A tractable network model and computational approach

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ARTICLE INFO

Article history:
Received 6 October 2011
Accepted 12 July 2012
Available online 20 July 2012

Keywords:
Supply chains
Nuclear medicine
Healthcare
Supply chain network design
Optimization
Variational inequalities
Generalized networks
Molybdenum
Time-sensitive products
Radioactive decay

ABSTRACT

In this paper, we develop a tractable network model and computational approach for the design of medical nuclear supply chains. Our focus is on the molybdenum supply chain, which is the most commonly used radioisotope for medical imaging utilized in cardiac and cancer diagnostics. This topic is of special relevance to healthcare given the medical nuclear product's widespread use as well as the aging of the nuclear reactors where it is produced. The generalized network model, for which we derive formulae for the arc and path multipliers that capture the underlying physics of radioisotope decay, includes total operational cost minimization, and the minimization of cost associated with nuclear waste discarding, coupled with capacity investment costs. Its solution yields the optimal link capacities as well as the optimal product flows so that demand at the medical facilities is satisfied. We illustrate the framework with a case study. The framework provides the foundation for further empirical research and the basis for the modeling and analysis of supply chain networks for other very time-sensitive medical products.

1. Introduction

Medical nuclear supply chains are essential supply chains in healthcare and provide the conduits for products used in nuclear medical imaging, which is routinely utilized by physicians for diagnostic analysis. For example, each day, 41,000 nuclear medical procedures are performed in the United States using technetium-99m, a radioisotope obtained from the decay of molybdenum-99. Such supply chains have unique features and characteristics due to the products' time-sensitivity along with their hazardous nature. In this paper, we take on the challenge of developing a model for supply chain network design of medical nuclear products, which captures some of the salient issues surrounding such supply chains today, from their complexity, to the economic aspects, the underlying physics of radioactive decay, and the inclusion of waste management. We focus on molybdenum-99 due to its importance in medical diagnostics, its time-sensitive nature, and the fact that there are only a handful of production and processing facilities for this radioisotope globally.

In order to appropriately ground our framework, we first describe the underlying features of medical nuclear supply chains, and provide the necessary background for their understanding. For example, to create an image for medical diagnostic purposes, a radioactive isotope is bound to a pharmaceutical that is injected into the patient and travels to the site or organ of interest. The gamma rays emitted by the radioactive decay of the isotope are then used to create an image of that site or organ (Berger et al., 2004). Technetium, ^{99m}Tc, which is a decay product of molybdenum-99, ^{99}Mo, is the most commonly used medical radioisotope, accounting for over 80% of the radioisotope injections and representing over 30 million procedures worldwide each year. Over 100,000 hospitals in the world use radioisotopes. (World Nuclear Association, 2011). In 2008, over 18.5 million doses of ^{99m}Tc were injected in the US with 2/3 of them used for cardiac exams, with the other uses including bone scans, functional brain imaging, sentinel-node identification, immunoscintigraphy, blood pool labeling, pyrophosphates for identifying heart damage, and sulfur colloids for spleen scans (Lantheur Medical Imaging, 2009). Through this most widely used medical radioisotope, health professionals can enable the earlier and more accurate detection of cardiac problems as well as cancer, the two most common causes of death (see Kochanek et al., 2011). It is estimated that the global market for medical isotopes is 3.7 billion US$ per year (Kahn, 2008).

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http://dx.doi.org/10.1016/j.ijpe.2012.07.008

The production cycle of ^{99m}Tc, typically, begins with the fission of highly enriched uranium, HEU, to produce ^{99}Mo, with a half-life of 66.7 h. The ^{99}Mo, in turn, decays to ^{99m}Tc, whose half-life is approximately 6 h. The relatively short half-life of ^{99m}Tc, as compared to metabolism and human activity, makes it a suitable isotope for imaging. In addition, the gamma rays that are emitted due to the ^{99m}Tc decay have roughly the same wavelength as common X-rays allowing detection by detectors similar to those used for medical X-rays.

The production of ^{99}Mo occurs at only nine reactors in the world, with one in Canada, five in Europe, one in Australia, one in South Africa, and one in Argentina (see OECD, 2010a). The reactors irradiate targets, aluminum blocks or foil containing uranium-235, ^{235}U, to produce multiple fissions products, including ^{99}Mo. The irradiated targets containing the ^{99}Mo are then shipped to processing facilities where the ^{99}Mo is extracted and purified. The extracted ^{99}Mo is further transported to generator manufacturing facilities. There, generators, which are containers of ^{99}Mo in a chemical form that allows easy extraction of ^{99m}Tc are produced. The generators, which are relatively radioactively safe, are then shipped to the hospitals and medical imaging facilities where the ^{99m}Tc is eluted by a saline solution and the pharmaceutical injections prepared and administered. Since the decay of a single atom of ^{99}Mo produces a single atom of ^{99m}Tc, the activity of the generator is determined by the quantity of the ^{99}Mo present.

Since ^{99}Mo decays with a 66.7 h half-life, approximately 99.9% of the atoms decay in 27.5 days, making its production, transportation, and processing all extremely time-sensitive. In fact, the production of ^{99}Mo is quantified in *Six-day curies end of processing* denoting the activity of the sample 6 days after it was irradiated to highlight this (see OECD, 2010a). In addition to the time-sensitivity, the irradiated targets are highly radioactive, significantly constraining transportation options between the reactor and the processing facilities to only trucks that can transport the heavily shielded transportation containers. While the extracted ^{99}Mo continues to be constrained by its decay, its shielding requirements are reduced, allowing for transportation by modes other than trucks, including by air (cf. de Lange, 2010).

Although the maximum possible production from current reactors in 2010 was well over twice the current demand, it has been predicted that, with a 5% annual growth rate for imaging, the demand will exceed the supply by the end of the decade. However, this assumes that all reactors are capable of irradiating the necessary targets at all times. Due to routine maintenance, unexpected maintenance, and shutdowns due to safety concerns, the actual supply has been much closer to the demand. In 2009, in fact, the demand exceeded the supply and created a worldwide shortage of ^{99}Mo. Furthermore, several of the reactors are reaching the end of their lifetimes, since they are 40 to over 50 years old (cf. OECD, 2010a, Seeverens, 2010). Between 2000 and 2010, there were six unexpected shutdowns of reactors used for medical imaging products due to safety concerns (Ponsard, 2010) with the Canadian one shutdown in May 2009 due to a leak in the reactor with its return to service more than a year later in August 2010.

It is also important to note that the number of processors that supply the global market is only four, and that they are located in Canada, Belgium, The Netherlands, and South Africa. Australia and Argentina produce bulk ^{99}Mo for their domestic markets but are expected to export small amounts in the future. Amazingly, there are parts of the world in which there are no processing facilities for ^{99}Mo, including the Unites States, parts of South America, and Japan. Such limitations in processing capabilities limit the ability to produce the medical radioisotopes from regional reactors since long-distance transportation of the product raises safety and security risks, and also results in greater decay of the product. The number of generator manufacturers, in turn, with substantial processing capabilities, is under a dozen (OECD, 2010a).

Furthermore, in 2016, the Canadian reactor is scheduled for complete shutdown, raising critical questions for supply chain network design, since its processing facility will also need to be shutdown (OECD, 2010a).

This paper is organized as follows. In Section 2, we develop the multitiered supply chain network design model for molybdenum, ^{99}Mo. The framework may be used, with minor modification, for other radioisotopes. We describe the various tiers of the supply chain network, beginning with the nuclear reactors, moving on to the processors, then on to the generator manufacturing facilities, and, finally, to the hospitals and medical facilities, where the medical radioisotopes are injected into the patients. The supply chain network is quite complex since it consists of multiple activities of production, transportation, and processing, coupled with the physics of the radioisotope and its decay, along with regulatory restrictions as to transportation, due to the hazardous nature of the medical nuclear product.

We model the supply chain network design problem as an optimization problem on a generalized network. We identify the specific losses on the links/arcs through the use of the time decay of the radioisotope. We consider total cost minimization associated with the operational costs, along with the waste management costs, since we are dealing with nuclear products. Medical nuclear waste management issues have not received much attention in recent reports (cf. OECD, 2010a). The model captures the investment in capacities through the construction of new links. Its solution provides the optimal investments along with the optimal levels of production, transportation, and processing, given the demands at the various hospitals and medical imaging facilities. We use a variational inequality formulation since such a formulation results in an elegant computational procedure. Moreover, the theory of variational inequalities has been applied to a plethora of supply chain modeling, analysis, and design problems (see Zhang, 2006; Nagurney, 2006, 2010; Qiang et al., 2009; Liu and Nagurney, 2011; Cruz and Liu, 2011). Furthermore, it provides a rigorous mathematical and computational framework to enable the exploration of alternative economic behaviors among the medical nuclear supply chain stakeholders, including competition (see Nagurney, 2006).

Such a modeling approach is in concert with recent studies that have focused on the security and reliability of medical nuclear supply chains that also emphasize that governments ultimately have the responsibility for establishing an environment conducive to investment in such supply chains (cf. OECD, 2010a). However, to the best of our knowledge, our model is the first mathematical one to include the operational, engineering, economic, and physics aspects of medical nuclear products. Indeed, the model is sufficiently general to capture the economic aspects of medical nuclear supply chain network design, which is an important issue since it has been recognized that usually governments run the reactors, which are research reactors, and the prices associated with the radioisotope may fail to capture the associated costs and, as a consequence, the pricing may be below marginal costs resulting in market failure; see OECD (2010a) and Seeverens (2010). For references to other generalized nonlinear network models and applications, see Nagurney and Aronson (1989), Nagurney et al. (2012), and the references therein. Nagurney and Masoumi (2012) recently developed a supply chain network design model for a sustainable blood banking system but the demands therein were uncertain. In our model and applications the demands are fixed since the associated medical procedures need to be scheduled.

In Section 3, we propose a computational approach for the new model, along with the accompanying theory, which resolves the