Abstract. We introduce a continuous stochastic model for the PSA (prostate-specific antigen) levels following radiotherapy and derive solutions for the associated partial differential (Kolmogorov-Chapman) equation. The solutions describe the evolution of the time-dependent density for PSA levels which take into account an absorbing condition along the boundary and various initial conditions. We include implications for single-dose and multi-dose radiation treatment regimens and discuss parameter estimation and sensitivity issues.

1991 Mathematics subject classification (Amer. Math. Soc.): 35K57, 60G51, 60H30, 60H35, 92B15

Keywords: PSA (prostate-specific antigen); Prostate cancer; Continuous stochastic model; Deterministic model; Stochastic differential equation; Chapman-Kolmogorov partial differential equation; Exponential decay; Method of images; Radiotherapy; Sensitivity analysis.
1. Introduction

Prostate cancer is one of the leading causes of deaths of American men over age 50. Although no treatment yet available provides a certain cure for this malignant disease, early detection of a developing tumor makes possible a significant improvement in clinical prognosis.

Prostate-specific antigen (PSA) is a serine protease isolated from extracts of prostate tissue and is a biomarker in the identification and treatment of prostate cancer. For normal men the PSA level is likely to be below 4, with elevated PSA levels considered as a possible indication of prostate cancer. One of the main treatments for this malignant disease is radiation therapy. In many situations the radiation is administered in small doses over a period of time in order to prevent excess damage to normal cells. In other cases a single application of radiation may be prescribed. After radiation treatment, monitoring of PSA levels is done to determine if the treatment has been successful. For patients whose PSA level again rises to a critical level, additional treatments or surgery are often undertaken.

Thus, knowledge of PSA movement following radiation is useful for monitoring treatment effectiveness and as an aid in the development of management policies for prostate cancer. We assume that PSA level serves as a biomarker for the post-treatment density of cancer cells (as detailed in [1] and [2]). Recent studies in [3]–[10] have focused on the applicability and limitations of deterministic models for post-treatment PSA levels. The authors of [11] describe the evolution of PSA level via the ordinary differential equation

\[ \frac{dx}{dt} = \alpha x - ke^{-at}, \]

where \( x(t) \) is the PSA level at time \( t \) and where \( \alpha > 0, a > 0 \) and \( k > 0 \). (\( \alpha \) and \( a \) capture, respectively, the intrinsic growth in tumor cells and the decay in cells due to treatment; \( k \) is an indicator of treatment intensity/effectiveness.) The ordinary differential equation (1.1) is subject to the initial condition \( x(0) = m \), where \( m > 0 \) is the PSA level just prior to radiation treatment. The
solution of this initial-value problem was shown in [11] to be

\[ x(t) = \left( m - \frac{k}{a + \alpha} \right) e^{\alpha t} + \left( \frac{k}{a + \alpha} \right) e^{-at}, \]  

where for \( t = 0 \) we have \( dx/dt = \alpha m - k \). In particular, if \( m < k/(a + \alpha) \), then (1.2) implies that the treatment is effective (no relapse); in that case the PSA level decreases to zero, and the cure time is \( T = (1/(a + \alpha)) \ln[k/(k - m(a + \alpha))] \) with \( x(t) = 0 \) for \( t \geq T \). One distraction of the deterministic model in this case is that, without further stipulation at the boundary, the solution given by (1.2) not only decreases to zero but then becomes negative. The stochastic model developed in §2, with its absorbing boundary, avoids this problem. If \( k/(a + \alpha) < m < k/\alpha \), then the treatment is effective only in the “short term”, i.e. the onset of relapse occurs in finite time \( T_1 = (1/(a + \alpha)) \ln[ka/(\alpha(m(a + \alpha) - k))] \). If \( m > k/\alpha \), then the treatment is ineffective. The deterministic solution is used in §3 to develop optimal treatment plans.

Other authors, including those of [1], [12], [13] have used models corresponding to (1.1). There is general agreement that the PSA level monitored over time following radiation therapy is an important indicator of the success or failure of the treatment. However, such deterministic models are not able to reflect the uncertainty in treatment outcome, particularly in those cases, for which parameter values suggest a late upsurge in PSA biomarker. A discrete stochastic model was developed in [11] to include random effects on PSA histories. The continuous stochastic model presented in this paper determines the complete distribution of future PSA levels (including probabilities of cure) in many cases where success or failure of the radiation treatment is somewhat difficult to ascertain from clinical observations. As a result, the probability of cure can be evaluated for various model assumptions.

The present work considers PSA level (more realistically) as a continuous random variable governed by a stochastic differential equation based on the assumptions in [11]. The diffusion process for the PSA level is developed in §2 and allows the solution to be expressed in analytical form for an important class of problems. In §3 we compare the probability of cure using the deterministic
model and the diffusion (stochastic) model, the latter exhibiting more insights into the real PSA level process following therapy. We also use new results from the deterministic model to suggest optimal treatment strategies. In §4 we discuss issues of parameter estimation and sensitivity, including the development of a conditional density function for PSA level based on prior observation.

2. CONTINUOUS STOCHASTIC MODEL

PSA level can be modeled as a continuous stochastic process \( \{X(t)\} \) satisfying a stochastic differential equation:

\[
\begin{align*}
dX(t) &= (\alpha X - ke^{-at})dt + \sigma dZ(t),
\end{align*}
\]

where \( dZ(t) \) is a Wiener process with zero mean and unit variance and \( \sigma \) is a constant “volatility” of the \( \{X(t)\} \) process. The forward Chapman-Kolmogorov partial differential equation (cf. [14]) associated with (2.1) is

\[
\begin{align*}
\frac{1}{2} \sigma^2 \frac{\partial^2 p}{\partial x^2} - \frac{\partial}{\partial x} (\alpha x - ke^{-at})p = \frac{\partial p}{\partial t}, \quad (x, t) \in \mathcal{R},
\end{align*}
\]

where \( p(x, t) : \mathcal{R} \mapsto \mathbb{R} \) is, for each \( t \in [0, \infty) \), the probability density function in \( x \), and where \( \mathcal{R} \equiv [0, \infty) \times [0, \infty) \). Then \( p(x, t)dx = \Pr\{X(t) \in (x, x + dx)\mid X(0) = m\} \). The deterministic initial condition \( x(0) = m \) may be expressed as

\[
\begin{align*}
p(x, 0) &= \delta_m(x),
\end{align*}
\]

where \( \delta_m(x) \) is the Dirac unit measure at \( m \). Further, we assume the existence of an “absorbing barrier” (cf. [15]) at \( x = 0 \) that yields the boundary condition

\[
\begin{align*}
p(0, t) &= 0 \quad \text{for all} \quad t > 0.
\end{align*}
\]
We introduce the following change of variables on $\mathcal{R}$:

$$y = \alpha \left( x - \frac{k}{a + \alpha} e^{-at} \right) e^{-at},$$

$$\tau = \frac{\alpha \sigma^2}{2} \left( 1 - e^{-2\alpha t} \right),$$

and we set

$$Q(y, \tau) = \frac{p(x, t) e^{\alpha t}}{\alpha}.$$

The partial differential equation (2.2) is then transformed (cf. §6) into the heat equation for $Q(y, \tau)$:

$$\frac{1}{2} \frac{\partial^2 Q}{\partial y^2} - \frac{\partial Q}{\partial \tau} = 0,$$

where $Q(y, \tau)$ is the transformed probability density function defined on the (transformed) region (cf. Figure 1)

$$\mathcal{T} \mathcal{R} = \left\{ (\tau, y) : 0 < \tau < \frac{\alpha \sigma^2}{2}, y^*(\tau) \leq y < \infty \right\},$$

with

$$y^*(\tau) = -\frac{\alpha k}{a + \alpha} \left( 1 - \frac{2\tau}{\alpha \sigma^2} \right) \frac{a + \alpha}{2\alpha}.$$

$Q(y, \tau)$ satisfies the (transformed) initial condition

$$Q(y, 0) = \delta_{m^*}(y), \quad \text{where} \quad m^* = \alpha \left( m - \frac{k}{a + \alpha} \right),$$

and the (transformed) boundary condition

$$Q(y^*(\tau), \tau) = 0, \quad \text{for} \quad 0 < \tau < \frac{\alpha \sigma^2}{2}.$$

Thus, the original problem for the PSA density, given by (2.2), (2.3) and (2.4) is equivalent to a problem for the heat equation given by (2.6), (2.8) and (2.9).

Motivated by work reported in [13] (Equation 1), we assume for the derivation below that $a = \alpha$. The authors of [13] conducted a 35-patient study on the PSA response to external beam radiation, showing the compatibility of this assumption with clinical findings. In addition, results for the case $a = \alpha$ provide an upper bound on solutions with $a < \alpha$. 
If $a = \alpha$, then the infinite curved trapezoid region $TR$ in (2.7) becomes the infinite rectilinear trapezoid (cf. Figure 2) given by

$$TTR = \left\{ (\tau, y) : 0 < \tau < \frac{\alpha \sigma^2}{2}, y^{**}(\tau) \leq y < \infty \right\}, \text{ where}$$

$$y^{**}(\tau) = -\frac{k}{2} \left( 1 - \frac{2\tau}{\alpha \sigma^2} \right).$$

Then (2.8) can be replaced with

$$Q(y, 0) = \delta_{m^{**}}(y), \text{ where } m^{**} = \alpha m - \frac{k}{2},$$

while (2.9) can be replaced with

$$Q(y^{**}(\tau), \tau) = 0, \text{ for } 0 < \tau < \frac{\alpha \sigma^2}{2}.$$

We use the method of images to find the fundamental solution $q(y, \tau; m^{**})$ of the differential equation (2.6) on the region (2.10) with unit mass at $m^{**}$ and with the boundary condition (2.12). We first note that the fundamental solution of (2.6) with unit mass at $m^{**}$ on \{$(\tau, y) : 0 < \tau < \infty, -\infty < y < \infty$\} is a $C^\infty([\tau_0, \infty) \times \mathbb{R})$ function for any $\tau_0 > 0$ and it can be written as

$$q^*(y, \tau; m^{**}) = \frac{1}{\sqrt{2\pi \tau}} e^{-\frac{(y - m^{**})^2}{2\tau}}.$$

The method of images suggests a solution of the form

$$q(y, \tau; m^{**}) = q^*(y, \tau; m^{**}) - e^{2m^{**}A} q^*(y, \tau; -m^{**} - k).$$

Now since (2.12) must hold, (2.14) implies that

$$q(y^{**}(\tau), \tau; m^{**}) = 0 \text{ for all } \tau > 0.$$

From (2.10) and from (2.13)–(2.15) we have

$$m^{**}A = \frac{km}{\sigma^2}.$$
and \(q(y, \tau; m^{**})\) solves the initial-boundary value problem consisting of (2.6), (2.11) and (2.15). It follows from (2.5) that

\[
p(x, t; m) = \alpha e^{-\alpha t} q \left( \frac{x - k}{2\alpha} e^{-\alpha t} \right) e^{-\alpha t}, \frac{\alpha \sigma^2}{2} (1 - e^{-2\alpha t}); \alpha m - \frac{k}{2} \right)
\]
solves the problem (2.2), (2.3), (2.4). Combining (2.13), (2.14), (2.16) and (2.17), we obtain an explicit formula for the evolving probability density of PSA levels:

\[
p(x, t; m) = \frac{e^{-\alpha t}}{\sqrt{\alpha \sigma^2 \pi (1 - e^{-2\alpha t})}} \left\{ -\frac{[(k/2) - \alpha m + e^{-\alpha t}(\alpha x - (k/2)e^{-\alpha t})]^2}{\alpha \sigma^2 (1 - e^{-2\alpha t})} \right\}, \quad x \geq 0.
\]

Figure 3 exhibits a typical evolution of \(p(x, t, m)\).

While the above analysis treats the case in which the initial PSA level \((m)\) is known, it is also possible that the initial PSA is a random variable with probability density \(f(m) \geq 0\) and \(\int_0^\infty f(m) \, dm = 1\). Then we can write the evolving probability density function of PSA levels as

\[
p(x, t) = \int_0^\infty p(x, t; m) f(m) \, dm.
\]

If the initial distribution is uniform, i.e.,

\[
f(m) = \begin{cases} \frac{1}{2d}, & m \in [m_0 - d, m_0 + d], \\ 0, & \text{otherwise}, \end{cases}
\]

with \(m_0 > d > 0\), then we have

\[
p(x, t) = \frac{e^{-\alpha t}}{2d} \left\{ \Phi \left( \sqrt{2} (u - u_0) \right) - \Phi \left( \sqrt{2} (u - v_0) \right) \right\} - \exp \left( -\frac{2k}{\sigma^2} e^{-\alpha t} x \right) \left\{ \Phi \left( \sqrt{2} (v + v_0) \right) - \Phi \left( \sqrt{2} (v + u_0) \right) \right\},
\]

(2.19)
where

\[
\begin{align*}
  u &= \frac{(k/2) + e^{-\alpha t}(\alpha x - (k/2)e^{-\alpha t})}{\sqrt{\alpha \sigma^2(1 - e^{-2\alpha t})}}, \\
  v &= \frac{e^{-2\alpha t}(k - e^{2\alpha t}k + 2e^{\alpha t}\alpha x)}{2\sqrt{\alpha \sigma^2(1 - e^{-2\alpha t})}}, \\
  u_0 &= \frac{\alpha(m_0 - d)}{\sqrt{\alpha \sigma^2(1 - e^{-2\alpha t})}}, \\
  v_0 &= \frac{\alpha(m_0 + d)}{\sqrt{\alpha \sigma^2(1 - e^{-2\alpha t})}},
\end{align*}
\]

and \(\Phi(\cdot)\) is the cumulative distribution function for the standard normal random variable.

3. Implications for Treatment: Deterministic and Stochastic Models

Single Treatment Regimen. Comparisons of results from the continuous deterministic and stochastic models suggest possibly different outcomes for the radiologic treatment of prostate cancer. We confine our attention to the (clinically relevant) case for which the deterministic model predicts short-term effectiveness of treatment followed by a relapse that will progress unabated without further treatment. The parameter constraint for this case is given by

\[
(3.1) \\
\frac{k}{(a + \alpha)} < m < \frac{k}{\alpha} \text{ or, equivalently, } \alpha m < k < (a + \alpha)m
\]

depending on whether the focus is on the initial PSA \(m\) in light of a fixed treatment level \(k\) or on the development of a treatment level \(k\) appropriate for a given \(m\).

Consistent with clinical findings that parameters \(a\) and \(\alpha\) are of the same order (see [13]), we have again taken \(a = \alpha\) in the development of findings reported below. For \(m = k/(2\alpha)\) at the low (less threatening) end of the constraint range, the deterministic model (1.2) describes certain cure. The stochastic model with time-dependent PSA density function given by (2.18) (with variance \(\sigma^2 = 1\) results in a cure with probability less than 0.51 (other parameter values in both models are identical: \(a = \alpha = 2, k = 60, \text{ and } m = k/(2\alpha) = 15\)). This would suggest that a higher-than-minimal dose should be considered for a single application of radiation to achieve a reasonably high success rate.
Figures 4A and 4B provide graphical comparisons of the deterministic and stochastic models in this case.

For values of \( m \) slightly higher (\( m = 16 \)), the deterministic model results in a temporary reduction in cancer until time \( t = \ln(15)/4 = 0.667 \), when relapse sets in while the stochastic model predicts a successful treatment in roughly 2.5 percent of cases, with the others experiencing unacceptably increased PSA levels as is true in the deterministic model.

For values of \( m \) at the top of the range (\( m > k/\alpha = 30 \) in our examples), the deterministic model shows an exponentially increasing PSA level (treatment unsuccessful). With these parameter values, the stochastic model is in agreement, showing a dramatic advance in the malignancy (with PSA levels around 100) with probability 1. Other examples reflecting the sensitivity of cure rates to model parameters are discussed in §4.

**Multiple Treatment Regimen.** Because of the deleterious effects of radiation, clinicians regularly seek to identify the minimal effective level for therapeutic radiology. For a given initial PSA level, \( m \), this search may often settle on values of \( k \) in the intermediate range, \( am < k < (a + \alpha)m \).

By taking advantage of the optimal (but not curative) drop in PSA levels we can introduce a function \( M_k(m) \), the minimal level of PSA, occurring at time \( t_{\text{min}}(m, k) = (1/(a + \alpha)) \ln[(ka)/(\alpha(m(\alpha + \alpha) - k))] \), after which time there is a relapse. Using the deterministic solution (1.2), we obtain

\[
M_k(m) = \frac{k}{\alpha} \left( \frac{\alpha(m(a + \alpha) - k)}{ak} \right) \frac{a}{a + \alpha}.
\]

We note that \( M_k(k/(a + \alpha)) = 0 \) and that \( k/\alpha \) is a fixed point of \( M_k \) with \( M_k'(k/\alpha) = 1 \) and \( M_k''(k/\alpha) = -\alpha^2/(ak) \). Thus, the fixed point \( k/\alpha \) is semi-stable (from above, repelling below).

Starting with a value of \( k \) in the interval \((ma, m(a + \alpha))\), iteration of the map \( m \rightarrow M_k(m) \) will then lead eventually to zero. To reach zero in \( n + 1 \) iterations (treatments) with a minimal dose \( k \) requires that \( M_k^{(n)}(m) = k^{(n)}/(a + \alpha) \), where the superscript \( (n) \) indicates the number of iterations. For example, to eradicate the cancer (PSA) in two treatments, we need a dose of size \( k^{(2)} \).
\( M_{k^{(2)}}(m) = k^{(2)}/(a + \alpha) \). It follows that

\[
(3.3) \quad k^{(2)} = \frac{m(a + \alpha)^2}{(a + \alpha) + a \left( \frac{\alpha}{a + \alpha} \right)^{\alpha/2}}.
\]

To use a smaller dose requires a larger number of treatments. For example, \( k^{(4)} \) solves the equation

\[
M_{k^{(4)}}(M_{k^{(4)}}(M_{k^{(4)}}(m)))) = k^{(4)}/(a + \alpha)
\]

and is given by

\[
(3.4) \quad k^{(4)} = \frac{m\alpha}{\left( \frac{\alpha}{(a + \alpha)^2} \right)^{(a + \alpha)/2} \left( a + \alpha + a \left( \frac{\alpha}{a + \alpha} \right)^{\alpha/2} \right)^{(a + \alpha)/2}}.
\]

We can follow the multi-dose regimen indicated for one, two, and four doses in Figure 5. We also note that this algorithm can be generalized to obtain a dose for any specified number of treatments.

In the selection of dose size and treatment regimen, it is not completely clear what the most therapeutically appropriate constraint should be. Possible candidates for such a constraint might be (a) to minimize the maximum individual dose, (b) to minimize the maximum total residual dose level, taking dosage decay into account, or (c) minimize the total (cumulative) dose divided by time to cure. Of course, in any case the treatment regimen must be effective.

4. Issues of Parameters Estimation and Sensitivity Analysis

Except for the stochastic parameter (volatility), \( \sigma \), the meaning and values of parameters used in the deterministic model (1.1) and stochastic model (2.1) are comparable. Studies reported in [12] and [13] were based on clinical observations and argued for models with (using the symbolism of §1 and §2) \( a = \alpha \) or \( a > \alpha \). Using an iterative non-linear regression technique, estimates from these studies for the common value of \( a \) and \( \alpha \) were 2.17 yr\(^{-1}\) and 2.83 yr\(^{-1}\), respectively. Because the case \( a = \alpha \) holds in many situations where the success or failure of radiation therapy may not be known for some time, a more discriminating analysis of the outcome available from the stochastic model may be especially helpful in this case.
The analytic solution for the evolving distribution of PSA level given in (2.18) allows such an
analysis, including a study of the sensitivity of model outcomes to two model parameters of interest,
\( \sigma \) and \( m \). Fixing parameters \( a = \alpha = 2 \) (as suggested above) and \( k = 60 \) (identifying treatment
intensity and consistent with data in [13]), the probability of cure was computed, based on (2.18) for
times \( t_2 \) and \( t_4 \), where \( t_n \) is the time at which the fraction \( 2^{-n} \) of the original treatment \( (k) \) remains.

From the results (reported in Table 1 for \( t_4 \)) it can be seen that the volatility has a modest negative
effect on the probability of cure for initial PSA levels below the critical value of \( m = k/(a + \alpha) = 15. \)

For levels of initial PSA greater than 15, increased volatility has a small positive effect, while for
\( m = 15 \), the impact of volatility is the greatest (and most positive). In contrast to the generally
modest effect of change in volatility, the impact on probability of cure of the initial PSA level \( m \) is
very significant for values of \( m \) near the critical value. As suggested in the Table 1, for a wide range
of volatilities, a change in initial PSA level from 14 to 16 can dramatically affect the likelihood of
cure.

Because an individual patient, with an individual tumor and individual treatment, may be iden-
tified with parameter values which are specific to that situation, it is important that parameter
estimates be carried out using individual patient data such as that provided by the University of
Michigan Medical Center and applied in [16]–[19]. However, observations for a given patient are not
independent, complicating the estimation process. One advantage of the stochastic model developed
in this paper is that it produces a distribution of current PSA level conditioned on the prior PSA
reading from the sequence of PSA observations. Specifically, if the random value of PSA at observa-
tion time \( t_i \) is \( x(t_i) \) and the corresponding transformed value (using (2.5)) is \( y_i \), then the conditional
probability density function for \( y_i \) can be derived as

\[
(4.1) \quad f(y_{i+1}|y_i) = \frac{\alpha e^{-\alpha t_i}}{\sqrt{2\pi(\tau_{i+1} - \tau_i)}} \exp \left\{ -\frac{(y_{i+1} - y_i)^2}{2\pi(\tau_{i+1} - \tau_i)} \right\} \left(1 - e^{B_i}\right),
\]

where

\[
B_i = -\frac{4am_i m_{i+1} e^{-\alpha(t_{i+1} + t_i)}}{\sigma^2(e^{-2\alpha t_i} - e^{-2\alpha t_{i+1}})},
\]
and $m_i = x(t_i)$ is the measured PSA level at time $t_i$, $i = 1, \ldots, n$, with $n$ being the total number of observations.

Future work is needed to develop methods of estimation and hypothesis testing procedures which will take advantage of the conditional density function (4.1).

5. Conclusion

The analysis of a new continuous stochastic model for the response to therapeutic radiation of developing prostate cancer presented by the authors allows advances on several fronts in the understanding and approach to treatment of this cause of significant mortality and morbidity in older men. In particular, the analytic solution proven for the evolving PSA density function in the (clinically recognized) case when $a = \alpha$ allows both quantitative and qualitative comparisons between the existing deterministic model and the more realistic stochastic model presented here. For example, realization that the stochastic model may result in a probability of cure of barely 50% for parameter values that result in a certain cure in the deterministic case can be helpful in determining a treatment protocol which will have increased effectiveness. In addition, a discrete dynamical systems approach based on the deterministic model has led to suggestions for multiple treatment patterns which may reduce the possibility of deleterious side effects from radiation therapy.

Another potential use for the model of PSA response to radiotherapy presented here is in the discussion of possible definition of treatment failure. In the spirit of [16], we plan to explore the conjecture that our stochastic model may help to identify more rapidly when a relapse in such cancers has occurred.

Mathematical methods, especially involving the complex transformation (2.5) and the use of the method of images to find the analytic solution mentioned above, may be helpful to others working on cancer models. For those parameter values that do not allow an analytic solution, the authors intend to develop numerical methods which can efficiently provide the same kind of model applications.
shown here in the case where \( a = \alpha \). Plans for the future also include continued investigation of parameter estimation and sensitivity issues that are discussed in §4.

6. Appendix

We note that the transformation in (2.5) is smooth for any \( t > 0 \). So we obtain

\[
p(x, t) = \alpha \sqrt{1 - \frac{2t}{\alpha\sigma^2}} Q(y, \tau),
\]

\[
\frac{\partial p}{\partial x}(x, t) = \alpha^2 \left(1 - \frac{2t}{\alpha\sigma^2}\right) \frac{\partial Q}{\partial y}(y, \tau),
\]

\[
\frac{\partial^2 p}{\partial x^2}(x, t) = \alpha^3 \left(1 - \frac{2t}{\alpha\sigma^2}\right)^{3/2} \frac{\partial^2 Q}{\partial y^2}(y, \tau),
\]

and

\[
\frac{\partial p}{\partial t}(x, t) = -\alpha^2 \sqrt{1 - \frac{2t}{\alpha\sigma^2}} Q(y, \tau)
\]

\[
-\alpha^2 \sqrt{1 - \frac{2t}{\alpha\sigma^2}} \left(y - \frac{ak}{a + \alpha} \left(1 - \frac{2t}{\alpha\sigma^2}\right) \frac{a + \alpha}{2\alpha} \right) \frac{\partial Q}{\partial y}(y, \tau)
\]

\[
+\alpha^3 \sigma^2 \left(1 - \frac{2t}{\alpha\sigma^2}\right)^{3/2} \frac{\partial Q}{\partial \tau}(y, \tau),
\]

leading to (2.6).

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$y = \frac{a k}{a + \alpha}$

$y_t = \frac{a k}{a + \alpha}$

Figure 1. Transformed region $TR$
Figure 2. Rectilinear transformed region $\mathcal{TTR}$
Figure 3. Time evolution described by $p(x, t, m)$
Deterministic Model: Treatment Success

Figure 4A.
Figure 4B.
Figure 5.
Table I: Projected Treatment Efficacy* (probability of cure)

<table>
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<tr>
<th>Initial PSA (m)</th>
<th>0.2</th>
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<th>1.4</th>
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</tr>
<tr>
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<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.02</td>
</tr>
</tbody>
</table>

*Other model parameter values are $a = \alpha = 2$ and $k = 60$.

Efficacy is determined at time $t = 1.4$, when the treatment effect is roughly one-sixteenth of its original size.