



A deterministic simulation study of embryo marker-assisted selection for age at first calving in Nellore (*Bos indicus*) beef cattle

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Abstract

We used deterministic simulation of four alternative multiple ovulation and embryo manipulation (MOET) closed nucleus schemes to investigate the benefits of using marker-assisted selection (MAS) of Nellore (*Bos indicus*) beef cattle embryos prior to transplantation to reduce the age at first calving (AFC). We found that MAS resulted in increased genetic gain as compared to selection without AFC quantitative trait loci (AFC-QTL) information. With single-stage selection the genetic response (GR) increased as follows: GR = 0.68% when the AFC-QTL explained 0.02 of the AFC additive genetic variance (σ_A^2); GR = 1.76% for AFC-QTL explaining 0.05 σ_A^2 ; GR = 3.7% for AFC-QTL explaining 0.1 σ_A^2 ; and GR = 55.76% for AFC-QTL explaining 0.95 σ_A^2 . At the same total selected proportion, two-stage selection resulted in less genetic gain than single stage MAS at two-years of age. A single stage selection responses of $\geq 95\%$ occurred with pre-selected proportions of 0.4 (0.1 σ_A^2 explained by AFC-QTL), 0.2 (0.3 σ_A^2 explained by AFC-QTL) and 0.1 (0.5 σ_A^2 explained by AFC-QTL), indicating that the combined use of MAS and pre-selection can substantially reduce the cost of keeping recipient heifers in MOET breeding schemes. When the number of recipients was kept constant, the benefit of increasing embryo production was greater for the QTL explaining a higher proportion of the additive genetic variance. However this advantage had a diminishing return especially for QTL explaining a small proportion of the additive genetic variance. Thus, marker assisted selection of embryos can be used to achieve increased genetic gain or a similar genetic response at reduced expense by decreasing the number of recipient cows and number of offspring raised to two-years of age.

Key words: age at first calving, beef cattle, marker-assisted selection, pre-selection, quantitative trait loci.

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Introduction

A major reproductive trait in beef cattle is age at first calving (AFC), which is related to sexual precocity and measures the time from the birth of a heifer to its first calving. A lower AFC has a positive impact on both economic and breeding aspects of cattle production, such as reduced costs of raising heifers and reduced female generation interval. Despite the importance of AFC, many breeding programs do not include this trait in the breeding goal because of its low heritability, sex-limited expression and antago-

nistic relationships with production traits (Frazier *et al.*, 1999; Nogueira, 2004, Forni and Albuquerque, 2005; Pereira *et al.*, 2006).

In recent years, dense genetic maps of DNA markers have become available for several species, including cattle (Barendse *et al.*, 1997; Bishop *et al.*, 1994). In livestock, the major goal of map construction is to dissect the genome to identify genes or chromosomal regions controlling the expression of economically important traits, often called quantitative trait loci (QTL). Numerous experiments have been conducted to detect QTL with promising results for several species, including milk yield and composition, disease resistance, reproduction, growth and carcass traits in beef and dairy cattle (Weller *et al.*, 1990; Van Der Beek *et al.*, 1995; Schrooten and Bovenhuis, 2002, Casas *et al.*,

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2004, Gonda *et al.*, 2004, Schnabel *et al.*, 2005, Stone *et al.*, 2005, Mizoguchi *et al.*, 2006).

Breeding programs which use marker assisted selection (MAS) can use information on QTL to improve the accuracy of early selection in, for example, heifers or embryos. Marker assisted selection can help to increase genetic response, especially for traits with low heritable, sex-limited traits and late or postmortem measurable traits (Lande and Thompson, 1990; Meuwissen and Van Arendonk, 1992; Brascamp *et al.*, 1993; Ruane and Coleau, 1996; Meuwissen and Goddard, 1996; Spelman *et al.*, 1999; Spelman and Bovenhuis, 1998; Mackinnon and Georges, 1998; Meuwissen *et al.*, 2001; Dekkers and Hospital, 2002, Williams, 2005, Powel and Norman, 2006, Spotter and Dist, 2006).

Advances in DNA technologies have also favored the development of several reproductive technologies, such as embryo transfer (ET), ovary pick-up (OPU), *in vitro* fertilization (IVF), *in vitro* production of oocytes derived from stem cells and cryopreservation. These techniques can be used to increase the number of embryos produced per cow and consequently the number of animals available for selection. Another research area of interest in embryo technology is the development of preimplantation genetic typing, also called preimplantation genetic diagnosis (PGD), which livestock breeders can use to predict phenotypic characteristics such as gender and production performance prior to embryo transfer and prevent transmission of genetic disorders. Preimplantation genetic diagnosis can be performed using single cells from biopsies and polymerase chain reaction (PCR) or fluorescent *in situ* hybridization (FISH) to determine gender or the presence of desired alleles in half-sib or full-sib embryos (Gomez-Raya and Klemetsdal, 1999, Bredbacka, 2001, Chrenek *et al.*, 2001, Abdel-Azim and Freeman, 2002, Stella *et al.*, 2002, Virta *et al.*, 2002, Hirayama *et al.*, 2004, Hansen and Block, 2004, Lee *et al.* 2004, Basrur and King, 2005, Mapletoft and Hasler, 2005, Hageyama *et al.* 2006).

There are various reports of livestock pregnancy rates of 30% to 60% when using biopsied embryos, similar to the rates obtained with intact embryos and considered sufficient for commercial applications (Agca *et al.*, 1998, Chrenek *et al.* 2001, Garcia, 2001, Lopes *et al.* 2001, Park *et al.* 2001, Chen *et al.* 2002, Tominaga, 2004, Tominaga and Hamada, 2004).

A multistage selection procedure that combines the favorable aspects of independent culling and index selection has been presented by Xu and Muir (1991). A multistage selection program can be optimized to maximize aggregated economic gain and incorporate genetic marker information, but the main advantage of multistage selection procedures over single-stage selection procedures is cost-saving (Xu *et al.*, 1995, Schulman and Dentine, 2005, Schrooten *et al.*, 2005). Multistage selection and marker assisted selection can be combined with preimplantation ge-

netic diagnosis by selecting embryos, produced by super ovulation or *in vitro* fertilization, prior to implantation, which allows the transfer of embryos with the highest predicted genetic value into recipient cows.

The aim of the study described in this paper was to analyze the expected genetic gain for age at first calving in Nellore cattle using different strategies for incorporating marker assisted embryo pre-selection into breeding schemes. The effects of the proportion of additive genetic variance explained by the QTL and the degree of pre-selection among embryos were studied.

Methods

Genetic and population model

We deterministically simulated marker assisted selection applied to a multiple ovulation and embryo manipulation *in vitro* fertilization (MOET-IVF) closed nucleus herd to improve AFC in Nellore *Bos indicus* cattle for a population with discrete generations. We evaluated two forms of marker assisted selection, single-stage selection (scheme A1, see below) using marker assisted selection at two years of age and two-stage selection (schemes A2, A3 and A4, see below) in which there was marker assisted selection of embryos in the first stage followed by a second-stage marker assisted selection of the animals at two years of age. In both cases we evaluated the AFC-QTL additive genetic variance (σ_a^2) in the range 0.00 to 0.95. The QTL information was included in the selection index as a correlated trait. Phenotypes (p_i) were the sum of breeding values (a_i) and environmental values (e_i), *i.e.* $p_i = a_i + e_i$, where a_i and e_i were assumed to be independent and normally distributed.

Age at first calving (AFC) was the only breeding goal trait and selection was based on breeding value best linear unbiased prediction, using an multi-trait animal model. Response to selection was predicted deterministically using the pseudo-BLUP selection index (Wray and Hill, 1989). The selection index included information on predicted dam AFC based on age at first ovulation, male scrotal circumference (SCR) and the AFC-QTL. The model assumed that the predicted AFC fully correlated with the actual AFC so that dams effectively had an AFC self-performance record. The AFC estimated breeding values for sires were based on SCR self-performance and AFC-QTL, sib information (full and half-sibs) on SCR, AFC and AFC-QTL, and full pedigree information. The estimated breeding values for dams were based on self-performance for AFC and AFC-QTL, sib information (full and half-sibs) on SCR, AFC and AFC-QTL, and full pedigree information. The type and amount of information used for each sex is summarized in Table 1. In the basal scheme, 30 sires and 120 dams were selected from each generation out of the 4,800 offspring produced (40 embryos per cow), implying a total selected proportion of 0.0125 for sires and 0.05 for dams. Dams and

calves were selected when 24 months old and had produced embryos and/or offspring for up to 6 months. No information on QTL was used in the basal scheme.

The effect of QTL information and pre-selection proportions on genetic gain was evaluated using four alternative schemes (Table 2). In scheme A1, sires and dams were selected at 2 years of age using all available information including the AFC-QTL data responsible for 0.00 (basal scheme) to $0.95 \sigma_A^2$. In schemes A2 and A3 embryos were pre-selected in the first stage based on AFC-QTL and pedigree information, while in second stage at 2 years of age genetic gain was based on the same information as was used in scheme A1. Scheme A2 investigated the effect of a varying degree of pre-selection in which the AFC-QTL data was responsible for 0.1, 0.3 or $0.5 \sigma_A^2$ and the pre-selected proportion of animals ranged from 0% to 100%, while scheme A3 studied the effect of a varying proportion of AFC-QTL σ_A^2 in which it was responsible for 0.02 to $0.95 \sigma_A^2$ and the pre-selected proportion of animals was fixed at 32.5%. Scheme A4 had a constant number 800 transferred embryos, considering a constant number of recipient cows, and an increasing number of embryos produced per dam (13 to 2000), the embryos being pre-selected based on AFC-QTL and full pedigree information. The number of selected embryos in the first stage from the total embryos produced and the number of animals selected in the second stage are given in Table 2.

Genetic gain rates were predicted deterministically using the SelAction program (Rutten *et al.*, 2002) employing advanced selection index theory to predict the genetic gain rates of breeding schemes by combining offspring generation phenotypic information with the estimated breeding values of the parent generation to produce an estimated breeding value for the selection candidate (Villa-

nueva *et al.*, 1993). Inclusion of estimated breeding values of the parent generation is the reason why pedigree information was included in the models, and allowed prediction of the response to selection using the BLUP-EBV animal model (Wray and Hill, 1989). The program accounts for the reduction of the additive genetic variance due to gametic-phase disequilibrium (the Bulmer effect, Bulmer 1971) and for reduction of the selection intensity due to correlated index values of relatives (Meuwissen, 1991).

The genetic and phenotypic parameters used in this work were obtained from the literature (Toelle and Robinson, 1985; Martins-Filho and Lobo, 1992, Ferraz and Eler, 2000, Pereira *et al.*, 2002, Forni and Albuquerque, 2005). It was assumed that $h_{QTLFCA}^2 = 1$, meaning that the QTL can be identified with certainty, and that the QTL-AFC effect was measured on the same scale as AFC so that the regression of AFC on the QTL value equaled one. Therefore, if the AFC-QTL explained a proportion p^2 of the additive genetic variance (σ_A^2), then the genetic correlation between AFC and the AFC-QTL equaled p , and the correlation between AFC-QTL and the AFC phenotype equaled $p h_{AFC}$, where h_{AFC} is the square root of the AFC heritability. The genetic correlation between the AFC-QTL and scrotal circumference equaled $p r_g$, where r_g is the genetic correlation between AFC and scrotal circumference. Likewise, the phenotypic correlation between scrotal circumference and the AFC-QTL equaled $p r_g h_{SCR}$, where h_{SCR} is the square root of the scrotal circumference heritability (Table 3).

Results and Discussion

The A1 scheme results are shown in Table 4, which shows the total response results as a percentage of the basal scheme (AFC-QTL effect = 0), the response due to selec-

Table 1 - Age at first calving (AFC) quantitative trait loci (QTL), scrotal circumference (SCR) for sires and dams in the two different stages of each scheme.

Source	Sires				Dams			
	Stage one	Stage two		Stage one	Stage two		AFC-QTL	
	AFC-QTL	AFC	SCR	AFC-QTL	AFC-QTL	AFC		SCR*
Self-Performance	Yes	No	Yes	Yes	Yes	Yes	No	Yes
Number of half-sibs	No	60	60	No	No	60	60	No
Number of full-sibs	No	20	19	No	No	19	20	No

*The SCR for dams refers to the SRC for the sire which serviced the dam.

Table 2 - The number of sires and dams selected in first and second selection stages of each scheme and the number of embryos produced.

Scheme	Sires		Dams		Embryos produced
	Selected at stage one	Selected at stage two	Selected at stage one	Selected at stage two	
A1	-	30	-	120	4800
A2	30 to 2400	30	120 to 2400	120	4800
A3	800	30	800	120	4800
A4	160	30	640	120	1560 to 240000

Table 3 - Heritability (diagonal), phenotypic (upper diagonal) and genetic correlations (lower diagonal) for age at first calving (AFC), scrotal circumference (SCR) and the AFC quantitative trait loci (AFC-QTL).

	AFC	SCR	AFC-QTL
AFC	0.15	0.4	0.15ρ*
SCR	0.45	0.45	0.20ρ [†]
AFC-QTL	ρ**	³ 0.45ρ [#]	1

*Phenotypic correlation between AFC and AFC-QTL ($h_{AFC}ρ = 0.15ρ$).
[†]Phenotypic correlation between SCR and AFC-QTL ($r_{g,AFC,SCR}h_{SCR} = 0.45 \times 0.45 \rho = 0.20\rho$).
 **Genetic correlation between AFC and AFC-QTL (square root of the QTL genetic variance).
[#]Genetic correlation between SCR and AFC-QTL ($r_{g,AFC,SCR}ρ = 0.45\rho$).

tion of dams and sires, the AFC breeding goal standard deviation (AFC STD) and the accuracy for sires and dams for AFC marker assisted selection at two years of age with the AFC-QTL explaining 0.00 to 0.95 σ_A^2 . It can be seen that the reduction of genetic variance due to selection (the Bulmer effect) increased with the proportion of the additive genetic variance explained by the QTL (Table 4). Without marker assisted selection the reduction of genetic variance due to selection was 20% but rose to 45% when the AFC-QTL explained 95% of the additive genetic variance, while the AFC additive genetic standard deviation (AFC-STD) decreased from 42 to 35 days. It therefore appears that using AFC-QTL marker assisted selection increased variance reduction due to selection and thus reduced the benefit of using the AFC-QTL. In spite of the reduction in variance, the genetic response increased with the proportion of variance explained by the AFC-QTL. As theoretically expected,

increased gain due to increased accuracy was larger than reduction of gain due to reduction of genetic variance (Dekkers and Hospital, 2002). Thus genetic gain with marker assisted selection was superior to the gain achieved in the basal scheme for all values of the proportion of variance explained by the AFC-QTL. Genetic gain for the basal scheme was 49.83 days (100%). Using marker assisted selection the response increased from 0.8% when the AFC-QTL explained 0.02 σ_A^2 up to 55.76% when the AFC-QTL explained 0.95 σ_A^2 . Accuracy increased from 0.513 to 0.981 for sires and from 0.543 to 0.955 for dams. Accuracy for dams was greater than for sires when there was little or no AFC-QTL effect because the dams had self-performance information for AFC while sires had self-performance information only on the correlated trait of scrotal circumference. As the AFC-QTL effect (*i.e.* the proportional AFC genetic variation explained by the QTL) increased the dams AFC performance information became less important and the scrotal circumference performance of the sires provided some supplementary information, consequently, the accuracy for sires became slightly higher than that for dams. The benefit of using marker assisted selection was, therefore, larger in regard to the selection of males than females. The genetic superiority of marker assisted selection over the basal scheme was 1.76% with the AFC-QTL explaining 0.05 σ_A^2 and 3.80% when the AFC-QTL explained 0.1 σ_A^2 , similar to the results obtained in other studies (Meuwissen and Goddard, 1996; Spelman and Van Arendonk, 1997).

Scheme A2 used marker assisted selection with embryo pre-selection with varying pre-selection rates. The percentage total response relative to single-stage selection

Table 4 - Scheme A1: Single-stage marker assisted selection. Age at first calving (AFC) quantitative trait locus (QTL) total response (TotResp); response due to selection of dams (RespDam) and sires (RespSire) as a percent of the basal scheme; AFC breeding goal standard deviation (AFC-STD) and the accuracy for sires and dams for single-stage marker assisted selection at two-years of age with the AFC-QTL explaining 0.00 to 0.95 of the additive genetic variance.

AFC-QTL Effect	TotResp	Respdam	Respsire	AFC-STD (days)	Sire accuracy	Dam accuracy
Basal Scheme*	100.0	100.0	100.0	41.98	0.513	0.543
0.02	100.8	100.4	100.7	41.84	0.518	0.547
0.05	101.8	101.3	102.2	41.79	0.525	0.552
0.1	103.8	102.6	104.5	41.69	0.539	0.562
0.2	108.2	106.1	110.1	41.51	0.570	0.585
0.3	113.7	110.0	116.5	41.07	0.607	0.614
0.4	119.3	114.7	123.6	40.53	0.650	0.649
0.5	125.7	119.9	130.7	39.89	0.699	0.689
0.6	132.1	125.5	137.8	39.14	0.752	0.736
0.7	138.8	131.2	145.3	38.30	0.810	0.789
0.8	145.4	137.2	152.4	37.38	0.872	0.847
0.9	152.2	143.7	159.6	36.37	0.943	0.916
0.95	155.8	147.2	163.3	35.23	0.981	0.955

*Using basal scheme (AFC-QTL effect = 0) the total response was 49.83 days and the response due to selection was 23.1 days for dams and 26.7 days for sires.

after two-stage marker assisted selection with the AFC-QTL explaining 0.1, 0.3 and 0.5 σ_A^2 is shown in Table 5. During the first stage, embryos were pre-selected based on the AFC-QTL, with the selected proportions ranging from all embryos transferred (100%) to selection performed fully at the embryo stage. As expected, the genetic gains with marker assisted pre-selection at the embryo stage were lower than the gains achieved with single-stage marker assisted selection. This effect was due to the loss of intensity at two-years old (when more information was available, *i.e.* self-performance for cows and full and half sibs), resulting in a smaller total selection differential. The greater the proportion of variance explained by the AFC-QTL the higher the selection accuracy and the lower the loss of genetic response due to pre-selection. The results show that it is possible to obtain responses higher than 95% of the response obtained with single-stage marker assisted selection, when using first-stage selected proportions of 0.4, 0.2 and 0.1 for AFC-QTL substitution effects of 0.1, 0.3 and 0.5 σ_A^2 respectively. These results suggest that it is possible to reach a satisfactory response by transferring only 10 to 40% of the collected embryos, thus reducing the total number of recipients without losing genetic gain. Therefore pre-selection at the embryo stage can be useful to reduce cost of the breeding program.

The A3 scheme investigated the response to marker assisted selection at the embryo stage with varying AFC-QTL. The total response, response as percentage of the basal scheme, the response due to selection of dams and sires, the AFC breeding goal standard deviation (AFC-STD) and the accuracy for sires and dams after two-stage

Table 5 - Scheme A2: Percentage total response for age at first calving (AFC) two-stage marker assisted selection at the embryo stage (embryo selection rate 0.0125 to 1) and at two-years old at additive genetic variance levels of 0.1, 0.3 and 0.5.

Pre-selection	Percentage total response for additive genetic variance levels of 0.1, 0.3 and 0.5		
	0.1	0.3	0.5
0.013	43.8	67.8	83.6
0.1	80.2	92.1	97.6
0.2	90.2	97.1	99.5
0.3	95.0	98.9	99.8
0.4	96.5	99.5	99.9
0.5	97.9	99.7	100.0
0.6	98.8	99.9	100.0
0.7	99.4	99.9	100.0
0.8	99.6	99.9	100.0
0.9	99.9	100.0	100.0
1.0*	100.0	100.0	100.0

*At two-years old without pre-selection the total response was 50 days, 55.4 days and 61.7 days for AFC-QTL substitution effect 0.1, 0.3, 0.5 additive genetic variance.

AFC marker assisted selection with the proportions of the additive genetic variance explained by the AFC-QTL ranging from 0 to 0.95 are shown in Table 6. For all the AFC-QTL effects, 40 embryos were generated and 13 transferred so that the pre-selected proportion equaled 32.5%, except for the basal scheme without pre-selection. The genetic gain for the basal scheme was 49.83 days (100%). For small proportions of variance explained by AFC-QTL the genetic gains with pre-selection were lower than those achieved in the basal scheme but became higher for AFC-QTL effects larger than 0.2 σ_A^2 . This was caused by reduced accuracy due to embryo pre-selection, which was counteracted by the proportion of variance explained by the AFC-QTL. The situation with the AFC-QTL effect identified as B-13 in Table 6 refers to the situation in which cows produced 13 embryos and no pre-selection was performed at the embryo stage. The production of 3.25 times more embryos (*i.e.* 40 instead of 13 embryos: the basal scheme *vs.* B-13) increased genetic gain by approximately 23%. Response improvement was due to increased selection intensity. Even using marker assisted selection with QTL effects explaining a small proportion (0.02, 0.05) of the additive genetic variance there was a larger response (9.0% and 12.6%, respectively) than that obtained when only 13 embryos were produced. In these situations the greater selection intensity compensated for the pre-selection losses.

Scheme A4 analyzed the response to marker assisted selection at the embryo stage with increased number of embryos. As shown in Table 6, marker assisted pre-selection can be used to reduce the costs related to raising offspring up to 2 years of age as well as maintenance of recipient cows. However, when producing more embryos, marker assisted pre-selection can also be used to increase response to selection compared to the basal scheme. Table 7 presents the percentage total response compared to the scheme with 13 embryos produced per cow for AFC-QTL 0.1, 0.3 and 0.5 σ_A^2 .

As expected, increasing the number of embryos produced and, consequently, first-stage selection intensity, resulted in higher genetic response in the three situations, with a diminishing return when more embryos were produced. The increased genetic response as a consequence of increased selection intensity was higher due to larger QTL effects. For larger QTL effects more embryos could be produced in order to obtain a higher first-stage selection intensity and, consequently, more compensatory responses.

Implications of the study

Improvement of reproductive techniques such as embryo transfer, *in vitro* fertilization, *in vitro* production of oocytes derived from stem cells and cryopreservation has increased the number of embryos produced per cow and, consequently, the number of offspring available for selection. The development of preimplantation genetic diagno-

Table 6 - Scheme A3: Two-stage marker assisted selection of embryos at stage 1 and two-year old dams and sires at stage 2. Age at first calving (AFC) quantitative trait locus (QTL) total response as a percent of the basal scheme; total response and response due to selection of dams and sires in days; AFC breeding goal standard deviation (AFC-STD) and the accuracy for sires and dams for two-stage marker assisted selection with the AFC-QTL explaining 0.00 to 0.95 of the additive genetic variance.

Equilibrium parameters							
AFC-QTL effect	Percentage response	Total response (days)	Dam response (days)	Sire response (days)	AFC-STD (days)	Sire accuracy	Dam accuracy
Basal scheme* [†]	100.0	49.83	23.10	26.70	41.8	0.513	0.543
B-13*	81.04	40.37	17.40	22.97	42.0	0.518	0.547
0.02	88.34	44.00	20.77	23.27	42.0	0.479	0.553
0.05	91.23	45.47	21.37	24.07	41.9	0.487	0.559
0.1	95.32	47.50	22.27	25.20	41.7	0.501	0.568
0.2	102.80	51.23	23.87	27.37	41.3	0.534	0.591
0.3	109.92	54.77	25.30	29.47	40.8	0.574	0.620
0.4	116.71	58.13	26.63	31.50	40.1	0.618	0.654
0.5	123.54	61.57	27.93	33.60	39.4	0.668	0.694
0.6	131.96	65.73	29.57	36.20	38.3	0.736	0.752
0.7	137.14	68.33	30.57	37.77	37.6	0.781	0.792
0.8	143.92	71.70	31.93	39.77	36.6	0.844	0.849
0.9	151.05	75.27	33.43	41.80	35.4	0.916	0.917
0.95	154.70	77.07	34.23	42.83	34.8	0.955	0.955

*The pre-selected proportion with marker assisted selection at the embryo stage was 32.5% (13 embryos selected and transferred from 40 embryos produced) except in the basal scheme (40 embryos produced per dam) and the B-13 scheme (13 embryos produced per dam) without pre-selection.

Table 7 - Scheme A4: Percentage total response for embryos per cow compared to the scheme in which 13 embryos were produced per cow (100%, first row) for the age at first calving quantitative trait locus (AFC-QTL) at additive genetic variance levels of 0.1, 0.3 and 0.5.

Embryos per cow	Percentage total response for additive genetic variance levels of 0.1, 0.3 and 0.5		
	0.1	0.3	0.5
13*	100.0	100.0	100.0
20	106.8	109.0	109.7
40	114.4	121.1	123.6
100	121.0	133.9	139.5
200	124.3	142.0	150.2
500	127.9	151.1	162.9
1000	129.9	158.0	173.0
2000	131.6	164.5	181.8

*At two-years old without pre-selection the total response was 39.1 days, 44.4 days and 49.7 days for AFC-QTL at additive genetic variance levels of 0.1, 0.3 and 0.5.

sis allows the pre-selection of embryos using marker information prior to transfer to recipient cows. Embryo pre-selection can be used to either increase genetic response or to reduce costs of the breeding program. The majority of costs in a MOET nucleus breeding program are due to the maintenance of recipient cows and the feeding of the growing animals until selection. Embryo pre-selection using marker assisted selection can substantially reduce the

costs by reducing the number of recipient cows and transferred embryos needed. Increased genetic gain could be obtained by increasing the number of embryos produced per cow and pre-selecting those with the desired QTL alleles. This would produce increased total selection intensity and, consequently, higher genetic gain without increasing (or even reducing) the number of recipient cows. The ideal number of embryos produced per cow and consequently the pre-selection rate is dependent on the proportion of the additive genetic variance explained by the QTL, the technical difficulties and the costs involved in producing, evaluating and transferring the embryos, as well as the benefits of implementing these breeding schemes.

These results suggest that marker assisted selection at the embryo stage can be used to enhance genetic response and reduce cost even with markers explaining a relatively small proportion (*e.g.* 0.05) of the additive genetic variance.

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